OLIGONUCLEOTIDE COMPOSITIONS AND METHODS THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[00001] This application claims priority to United States Provisional Application Nos. 63/575,619, filed on April 5, 2024, 63/714,113, filed on October 30, 2024, and 63/770,940, filed on March 12, 2025, the entirety of each of which is incorporated herein by reference.

BACKGROUND

[00002] Oligonucleotides are useful in various applications, e.g., therapeutic, diagnostic, and/or research applications. For example, oligonucleotides targeting various genes can be useful for treatment of conditions, disorders or diseases related to such target genes, e.g., PNPLA3.

SUMMARY

[00003] Many conditions, diseases or disorders are associated with PNPLA3 and/or mutations thereof. For example, various conditions, diseases or disorders are associated with I148M PNPLA3 mutation. Homozygous individuals with I148M PNPLA3 mutation can have higher risks of various conditions, diseases or disorders, and in some cases, of early death caused by liver conditions, diseases or disorders. Technologies have been developed to knockdown or knockout PNPLA3, in some cases, targeting both wild-type and mutant PNPLA3, and in some cases, selectively targeting mutant PNPLA3.

[00004] Among other things, the present disclosure encompasses the recognition that reported PNPLA3 knockdown or knockout technologies can suffer from various shortcomings. For example, in some embodiments, PNPLA3 knockdown or knockout can be worse than PNPLA3-I148M homozygous and/or heterozygous genotypes, e.g., in view of increased steatosis, increased lipid accumulation, and/or increased susceptibility to toxicity (e.g., to ethanol and/or methotrexate toxicity). Among other things, the present disclosure provides the insight that conversion of I148M PNPLA3 to I148V PNPLA3, e.g., through base editing of A·T to G·C in DNA (e.g., genomic DNA), through A to I RNA editing, etc., can provide PNPLA3 polypeptides with improved properties and/or activities, and can are useful for various applications including for treating various conditions, diseases or disorders.

[00005] Various technologies can be utilized in accordance with the present disclosure to edit an A in a codon for I148M in PNPLA3 to a codon for V. In some embodiments, a technology edits DNA. In some embodiments, a technology edits genomic DNA. In some embodiments, a technology edits an A genomic DNA. In some embodiments, a technology edits a transcript, e.g., a PNPLA3 RNA.

[00006] For example, in some embodiments, the present disclosure provides oligonucleotides that can edit the I148M codon in a PNPLA3 transcript to a codon for V. In some embodiments, the present disclosure provides PNPLA3 oligonucleotides and compositions thereof that have significantly improved properties and/or high activities. Among other things, the present disclosure provides technologies for designing,

preparing, and utilizing such oligonucleotides and compositions. Particularly, in some embodiments, the present disclosure provides oligonucleotides comprising useful patterns of internucleotidic linkages and/or patterns of sugar modifications, which, when combined with one or more other structural elements, e.g., base sequence (or portion thereof), nucleobase modifications (and patterns thereof), additional chemical moieties, etc., can provide PNPLA3 oligonucleotides and compositions thereof with high activities and/or desired properties, including, but not limited to, effective and efficient site-directed editing of a PNPLA3 transcript. In some embodiments, PNPLA3 oligonucleotides and compositions modify one or more A residues, such as through conversion of A to I. In some embodiments, PNPLA3 oligonucleotides and compositions modify an A residue (e.g., converting an A to an I) in a PNPLA3 transcript, producing an alternative amino acid residue in PNPLA3 transcript.

[00007] In some embodiments, the present disclosure provides PNPLA3 nucleic acid sequences (e.g., RNA) comprising an A to I variation (e.g., at a target adenosine), wherein I is read as G during translation. In some embodiments, PNPLA3 nucleic acid sequences comprise an A to I variation that is read as a G, wherein G form encodes one or more proteins with higher desired activities and/or one or more better desired properties compared to those encoded by the corresponding A form. In some embodiments, a target adenosine is located at a position in a PNPLA3 nucleic acid that encodes for a methionine (e.g., corresponding to position 148 of SEQ ID NO: 2). In some embodiments, a target adenosine is located at a position in a PNPLA3 nucleic acid that encodes for an isoleucine (e.g., corresponding to position 148 of SEQ ID NO: 2). In some embodiments, a G form of a PNPLA3 nucleic acid sequence encodes for a valine (e.g., corresponding to position 148 of SEQ ID NO: 2). In some embodiments, a PNPLA3 nucleic acid sequence is GCUUCIUSCCUUUCUAC, wherein S is either G or C and each U can be optionally and independently replaced with T. In some embodiments, a PNPLA3 nucleic acid sequence has about or at least about 10%, 20%, 30%, 40%, or 50% sequence identity to GCUUCGUGCCUUUCUACAGUGGCCUUAUCC, wherein each U can be optionally and independently replaced with T. In some embodiments, a PNPLA3 nucleic acid sequence has about or at least about 10%, 20%, 30%, 40%, or 50% sequence identity to GCUUCGUCCCCUUCUACAGUGGCCUUAUCC, wherein each U can be optionally and independently replaced with T. In some embodiments, a PNPLA3 nucleic acid sequence is codon optimized for expression in a cell.. In some embodiments, a cell is a mammalian cell. In some embodiments, a cell is a human cell.

[00008] In some embodiments, a PNPLA3 nucleic acid sequence encodes VDALVCSCFVPF. In some embodiments, a PNPLA3 nucleic acid sequence comprises an amino acid sequence with about or at least about 10%, 20%, 30%, 40%, or 50% sequence identity to VDALVCSCFVPF. In some embodiments, a PNPLA3 nucleic acid sequence comprises an amino acid sequence with about or at least about 10%, 20%, 30%, 40%, or 50% sequence homology to VDALVCSCFVPF.

[00009] In some embodiments, the present disclosure provides PNPLA3 polypeptide sequences comprising a valine at a position corresponding to position 148 of SEQ ID NO: 2. In some embodiments, a PNPLA3 polypeptide comprises SEQ ID NO:2 or a characteristic portion thereof. In some embodiments, a

PNPLA3 polypeptide is a characteristic portion of SEQ ID NO: 2 comprising V148. In some embodiments, a polypeptide comprises a characteristic portion of SEQ ID NO: 2, which characteristic portion comprises V148. In some embodiments, a characteristic portion can differentiate a PNPLA3 polypeptide from another polypeptide. In some embodiments, a characteristic portion can differentiate SEQ ID NO: 2 from another polypeptide. In some embodiments, a characteristic portion can differentiate SEQ ID NO: 2 from another polypeptide encoded by another gene. In some embodiments, a characteristic portion can differentiate SEQ ID NO: 2 from another polypeptide encoded by all other genes. In some embodiments, a polypeptide can provide one or more functions of a wild-type PNPLA3 polypeptide. In some embodiments, a polypeptide can provide high levels of functions, e.g., of a wild-type PNPLA3 polypeptide, compared to a reference polypeptide. In some embodiments, a reference polypeptide has M148 instead of V148 but is otherwise identical.

[00010] In some embodiments, the present disclosure provides cells comprising one or more PNPLA3 nucleic acids or polypeptides disclosed herein. In some embodiments, cells comprise a PNPLA3 nucleic acid comprising a sequence of GCTTCATGCCTTTCTACAGTGGCCTTATCC. In some embodiments, cells further comprise a PNPLA3 nucleic acid comprising a sequence of GCTTCATCCCCTTCTACAGTGGCCTTATCC. In transcripts (e.g., mRNA), T is typically U. In some embodiments, cells comprise a PNPLA3 nucleic acid comprising a sequence of GCUUCAUCCCCUUCUACAGUGGCCUUAUCC. In some embodiments, cells further comprise GCUUCAUGCCUUUCUACAGUGGCCUUAUCC. In some embodiments, cells further comprise a PNPLA3 polypeptide comprising a I148M variation, wherein position 148 is or corresponds to position 148 of SEQ ID NO: 2. In some embodiments, cells comprise a PNPLA3 polypeptide comprising an amino acid sequence of VDALVCSCFMPF. In some embodiments, a cell is a human cell.

[00011] In some embodiments, the present disclosure provides methods for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof, comprising modifying an amino acid residue at a position that is or correspond to position 148 of SEQ ID NO: 2. In some embodiments, methods comprise modification of a methionine. In some embodiments, methods comprise modification of an isoleucine. In some embodiments, increased lipase activity is about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 fold of that without a modification. In some embodiments, lipase activity is increased as compared to that of a PNPLA3 polypeptide comprising M148, wherein position 148 is or corresponds to position 148 of SEQ ID NO: 2. In some embodiments, lipase activity is increased as compared to that of a PNPLA3 polypeptide comprising I148, wherein position 148 is or corresponds to position 148 of SEQ ID NO: 2.

[00012] In some embodiments, the present disclosure provides oligonucleotides capable of editing a target adenosine in a nucleic acid encoding a PNPLA3 polypeptide to produce a PNPLA3 polypeptide variant that differs by at least one amino acid residue. In some embodiments, a target adenosine is at a position within a PNPLA3 nucleic acid corresponding to a codon encoding for an amino acid at position 148 of SEQ ID NO: 1

or 2. In some embodiments, an amino acid at position 148 is methionine. In some embodiments, an amino acid at position 148 is isoleucine.

[00013] In some embodiments, the present disclosure provides oligonucleotides capable of hybridizing to a target sequence comprising GCUUCAUSCCUUUCUAC, wherein S is either G or C. In some embodiments, oligonucleotides are capable of hybridizing to a target sequence comprising GCUUCAUGCCUUUCUAC. In some embodiments, oligonucleotides are capable of hybridizing to a target sequence comprising GCUUCAUCCCUUUCUAC. In some embodiments, a target sequence is a PNPLA3 transcript.

[00014] In some embodiments, the present disclosure provides oligonucleotides comprising a base sequence comprising at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is identical with or complementary to a base sequence of a PNPLA3 gene or a transcript thereof, wherein the oligonucleotide comprises one or more modified sugars, one or more modified nucleobases, and/or one or more modified internucleotidic linkages. In some embodiments, a base sequence of the oligonucleotide sequence comprises at least 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is complementary to a PNPLA3 transcript. In some embodiments, a base sequence comprises at least 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is complementary to a PNPLA3 mRNA. In some embodiments, oligonucleotides comprise a base sequence comprising at least 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 contiguous bases of GGAUAAGGCCACUGUAGAAGGGGAUGAAGC, GGGACACGGUGAUGGAGAAGGGCAUGAAGC, AUAAGGCCACUGUAGAAGGGGAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGGAUGAAGC, AGGGAUAAGGCCACUAGAAGGGGAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGGAUGAAGC, GGAUAAGGCCACUGUAGAAGGGCAUGAAGC, GAUAAGGCCACUGUAGAAGGGCAUGAAGCA, AUAAGGCCACUGUAGAAGGGCAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGCAUGAAGC, AGGGAUAAGGCCACUAGAAGGGCAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCAUGAAGC, GAUAAGGCCACUGUAGAAAGGCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, AUAAGGCCACUGUAGAAAGGCAUGAAGCAG, UAAGGCCACUGUAGAAAGGCAUGAAGCAGG, AAGGCCACUGUAGAAAGGCAUGAAGCAGGA, GGAUAAGGCCACUGUAGAAAGCCAUGAAGC, GGAUAAGGCCACUGUAGAAACGCAUGAAGC, GGAUAAGGCCACUGUAGAAUGGCAUGAAGC, GGAUAAGGCCACUGUAGAUAGGCAUGAAGC, GGAUAAGGCCACUGUAGUAAGGCAUGAAGC, GGAUAAGGCCACUGUACAAAGGCAUGAAGC, GGAUAAGGCCACUGUUGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCGUGAAGC, GGAUAAGGCCACUGUAGAGAGGCAUGAAGC, GGAUAAGGCCACUGUAGGAAGGCAUGAAGC, GGAUAAGGCCACUGUGGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGGGAGGCAUGAAGC, GGAUAAGGCCACUGUGGGGAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGUAUGAAGC, GGAUAAGGCCACUGUAGAAGGGUAUGAAGC, GGAUAAGGCCACUGUGGAAAGGUAUGAAGC,

GGGAUAAGGCCACUGUAGAAAGGCAUGAAGCA, or GGAUAAGGCCACUGUAGAAAGGCAUGAAGCAG, wherein each T can be independently replaced with U and vice versa.

[00015] Among other things, the present disclosure provides designed oligonucleotides and compositions thereof which oligonucleotides comprise modifications (e.g., modifications to nucleobases sugars, and/or internucleotidic linkages, and patterns thereof) as described herein. In some embodiments, technologies (compounds (e.g., oligonucleotides), compositions, methods, etc.) of the present disclosure (e.g., oligonucleotides, oligonucleotide compositions, methods, etc.) are particularly useful for editing nucleic acids, e.g., site-directed editing in nucleic acids (e.g., editing of target adenosine). In some embodiments, as demonstrated herein, provided technologies can significantly improve efficiency of nucleic acid editing, e.g., modification of one or more A residues, such as conversion of A to I. In some embodiments, the present disclosure provides technologies for editing (e.g., for modifying an A residue, e.g., converting an A to I) in an RNA. In some embodiments, the present disclosure provides technologies for editing (e.g., for modifying an A residue, e.g., converting an A to an I) in a transcript, e.g., mRNA. Among other things, provided technologies provide the benefits of utilization of endogenous proteins such as ADAR (Adenosine Deaminases Acting on RNA) proteins (e.g., ADAR1 and/or ADAR2), for editing nucleic acids, e.g., for modifying an A. Those skilled in the art will appreciates that such utilization of endogenous proteins can avoid a number of challenges and/or provide various benefits compared to those technologies that require the delivery of exogenous components (e.g., proteins (e.g., those engineered to bind to oligonucleotides (and/or duplexes thereof with target nucleic acids) to provide desired activities), nucleic acids encoding proteins, viruses, etc.).

[00016] Particularly, in some embodiments, oligonucleotides of provided technologies comprise useful sugar modifications and/or patterns thereof (e.g., presence and/or absence of certain modifications), nucleobase modifications and/or patterns thereof (e.g., presence and/or absence of certain modifications), internucleotidic linkages modifications and/or stereochemistry and/or patterns thereof [e.g., types, modifications, and/or configuration (Rp or Sp) of chiral linkage phosphorus, etc.], etc., which, when combined with one or more other structural elements described herein (e.g., additional chemical moieties) can provide high activities and/or various desired properties, e.g., high efficiency of nucleic acid editing, high selectivity, high stability, high cellular uptake, low immune stimulation, low toxicity, improved distribution, improved affinity, etc. In some embodiments, provided oligonucleotides provide high stability, e.g., when compared to oligonucleotides having a high percentage of natural RNA sugars utilized for adenosine editing. In some embodiments, provided oligonucleotides provide high activities, e.g., adenosine editing activity. In some embodiments, provided oligonucleotides provide high selectivity, for example, in some embodiments, provided oligonucleotides provide selective modification of a target adenosine in a target nucleic acid over other adenosine in the same target nucleic acid (e.g., 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 fold or more modification at the target adenosine than another adenosine, or all other adenosine, in a target nucleic acid).

[00017] Among other things, the present disclosure provides designed oligonucleotides and compositions of improved properties and/or activities compared to reference oligonucleotides and compositions (e.g., those described herein or reported in the art). For example, in some embodiments, as demonstrated herein provided oligonucleotide and compositions can provide improved stability, pharmacokinetic properties, pharmacodynamic properties and/or improved activities (e.g., for A-to-I editing). Various designed oligonucleotides and compositions are described herein. For example, in some embodiments, the present disclosure provides oligonucleotides and compositions thereof, including chirally controlled oligonucleotide compositions thereof, wherein the oligonucleotides comprise several (e.g., 1, 2, 3, 4, or 5 or more; in some embodiments, 3 or more) nucleosides independently comprising sugar modifications (e.g., 2'-OR modifications wherein R is optionally substituted C_{1-6} alkyl (e.g., 2'-OMe, 2'-MOE, etc.,), bicyclic sugars (e.g., LNA sugars, cEt sugars, etc.)) at their 5'- and 3'-ends. In some embodiments, the first several (e.g., 1, 2, 3, 4, or 5 or more; in some embodiments, 3 or more) nucleosides and/or the last several (e.g., 1, 2, 3, 4, or 5 or more; in some embodiments, 3 or more) nucleosides independently comprise sugar modifications. In some embodiments, the first 3 or more and the last 3 or more nucleosides independently comprise sugar modifications. In some embodiments, one or more internucleotidic linkages bonded to such nucleosides are non-negatively charged internucleotidic linkage such as phosphoryl guanidine internucleotidic linkages like n001. In some embodiments, both the first and the last internucleotidic linkages are independently non-negatively charged internucleotidic linkages. In some embodiments, both the first and the last internucleotidic linkages are independently phosphoryl guanidine internucleotidic linkages. In some embodiments, both the first and the last internucleotidic linkages are independently n001. In some embodiments, they are both chirally controlled and are *R*p. In some embodiments, an oligonucleotide comprises a nucleoside N_0 which comprises a natural DNA sugar (two 2'-H), a natural RNA sugar or a 2'-F modified sugar. In some embodiments, N_0 is a nucleoside opposite to a target adenosine when an oligonucleotide is utilized for adenosine editing. In some embodiments, sugar of N_0 is a natural DNA sugar. In some embodiments, sugar of N_1 ("+" or nothing before a number indicates counting toward the 5'-direction (5' ...$N_1N_0N_{-1}$... 3')) is a 2'-Fmodified sugar, a natural DNA sugar, or a natural RNA sugar. In some embodiments, sugar of N_1 is a DNA sugar. In some embodiments, sugar of N_{-1} ("-" indicates counting toward the 3'-direction (5' ...$N_1N_0N_{-1}$... 3')) is a 2'-F modified sugar, a natural DNA sugar, or a natural RNA sugar. In some embodiments, sugar of N_{-1} is a DNA sugar. In some embodiments, sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, between N_2 and their 5'-ends oligonucleotides comprise multiple 2'-F modified sugars and multiple 2'-modified sugars (e.g., 2'-OR modified sugars wherein R is optionally substituted C_{1-6} alkyl, bicyclic sugars such as LNA sugars, cEt sugars, etc.). In some embodiments, oligonucleotides comprise one or more (e.g., 1-20, 1-15, 1-10, 2-15, 2-10, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) 2'-F blocks and one or more (e.g., 1-20, 1-15, 1-10, 2-15, 2-10, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) separating blocks from N_2 to their 5'-ends (e.g., first domains and first subdomains of second domains combined when first subdomains end with and include N_2), wherein each nucleoside in a 2'-F block

independently comprises a 2'-F modification, each nucleoside in a separating block independently comprises no 2'-F modification, and each block independently comprises one or more (e.g., 1-20, 1-15, 1-10, 2-15, 2-10, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) nucleosides. In some embodiments, there are two or more such 2'-F blocks and two or more such separating blocks. In some embodiments, one or more or all such separating blocks are independently bonded to two 2'-F blocks. In some embodiments, each nucleoside in one or more or all separating blocks independently comprise a 2'-OR modification wherein R is optionally substituted C_{1-6} alkyl or is a bicyclic sugar such as a LNA sugar, a cEt sugar, etc. In some embodiments, each nucleoside in one or more or all separating blocks independently comprise a 2'-OR modification wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, each nucleoside in one or more or all separating blocks independently comprise a 2'-OMe or 2'-MOE modification. In some embodiments, each of such 2'-F and separating blocks independently comprises 1, 2, 3, 4 or 5 nucleosides. In some embodiments, nucleosides close to N_0, e.g., N_2, N_1, N_0, N_{-1}, N_{-2}, etc., do not contain large 2'-modificatoins such as 2'-MOE. In some embodiments, sugars of N_2, N_1, N_0, N_{-1}, and N_{-2} are independently natural DNA sugar, 2'-F modified sugar, or 2'-OMe modified sugar. In some embodiments, sugars of N_1, N_0, N_{-1} are each a natural DNA sugar. In some embodiments, each chiral internucleotidic linkage is independently chirally controlled.

[00018] In some embodiments, the present disclosure provides an oligonucleotide comprising a first domain and a second domain, wherein the first domain comprises one or more 2'-F modifications, and the second domain comprises one or more sugars that do not have a 2'-F modification. In some embodiments, an oligonucleotide comprises a modified nucleobase, nucleoside, sugar or internucleotidic linkage as described in the present disclosure. In some embodiments, about or at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% of all sugars in an oligonucleotide are 2'-F modified sugars.

[00019] In some embodiments, a second domain comprises or consists of a first subdomain, a second subdomain and/or a third subdomain as described herein. In some embodiments, an oligonucleotide comprises a second subdomain.

[00020] In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars and/or one or more modified internucleotidic linkages, wherein the oligonucleotide comprises a first domain and a second domain each independently comprising one or more nucleobases.

[00021] In some embodiments, when an oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, a target adenosine in the target PNPLA3 transcript is modified. In some embodiments, when an oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of the target PNPLA3 transcript is reduced compared to absence of the product or presence of a reference. In some embodiments, when an oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of a product of the target PNPLA3 transcript is altered compared to absence of the product or presence of a reference oligonucleotide. In some embodiments, a target PNPLA3 transcript is modified. In some embodiments, level of a product is increased, wherein the

product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is modified. In some embodiments, level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is replaced with inosine. In some embodiments, level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the adenine of the target adenosine is replaced with guanine. In some embodiments, a product is a protein. In some embodiments, a product is a PNPLA3 protein.

[00022] In some embodiments, a target adenosine is more associated with a condition, disorder or disease than a guanine at the same position. In some embodiments, an oligonucleotide is capable of forming a double-stranded complex with the target PNPLA3 transcript. In some embodiments, a target PNPLA3 transcript or a portion thereof is or comprises RNA. In some embodiments, a target adenosine is of an RNA. In some embodiments, a target adenosine is modified, and the modification is or comprises deamination of the target adenosine. In some embodiments, a target adenosine is modified and the modification is or comprises conversion of the target adenosine to an inosine. In some embodiments, a modification is promoted by an ADAR protein. In some embodiments, a system is an *in vitro* or *ex vivo* system comprising an ADAR protein. In some embodiments, a system is or comprises a cell that comprises or expresses an ADAR protein. In some embodiments, a system is a subject comprising a cell that comprises or expresses an ADAR protein. In some embodiments, a ADAR protein is ADAR1. In some embodiments, a ADAR protein is ADAR2.

[00023] In some embodiments, an oligonucleotide has a length of about 10-200 (e.g., about 10-20, 10-30, 10-40, 10-50, 10-60, 10-70, 10-80, 10-90, 10-100, 10-120, 10-150, 20-30, 20-40, 20-50, 20-60, 20-70, 20-80, 20-90, 20-100, 20-120, 20-150, 20-200, 25-30, 25-40, 25-50, 25-60, 25-70, 25-80, 25-90, 25-100, 25-120, 25-150, 25-200, 30-40, 30-50, 30-60, 30-70, 30-80, 30-90, 30-100, 30-120, 30-150, 30-200, 10, 20, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 60, etc.) nucleobases. In some embodiments, a base sequence of an oligonucleotide is complementary to a base sequence of a portion of a target PNPLA3 transcript comprising the target adenosine with 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches which are not Watson-Crick base pairs. In some embodiments, one or more mismatches are independently a wobble base paring. In some embodiments, complementarity is about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.). In some embodiments, complementarity is about 90%-100% or about 95-100%. In some embodiments, complementarity is 100%. In some embodiments, complementarity is 100% except at a nucleoside opposite to a target nucleoside (e.g., adenosine).

[00024] In some embodiments, an oligonucleotide can hybridize to a PNPLA3 transcript, wherein the

portion the oligonucleotide hybridize to comprises a target adenosine. In some embodiments, an oligonucleotide can hybridize to a PNPLA3 transcript, wherein the portion the oligonucleotide hybridize to is, comprises, overlaps with, or is gcttcatccccttctacagtggccttatcc or gcttcatgcctttctacagtggccttatcc. In transcripts (e.g., mRNA) T is typically U. In some embodiments, an oligonucleotide can hybridize to a PNPLA3 transcript, wherein the portion the oligonucleotide hybridize to is, comprises, overlaps with, or is gcuucaucccccuucuacaguggccuuaucc or gcuucaugccuuucuacaguggccuuaucc.

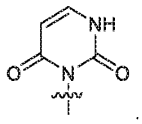
[00025] In some embodiments, an oligonucleotide consists of a first domain and a second domain. In some embodiments, a first domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a first domain has a length of about 10-25 nucleobases. In some embodiments, a first domain has a length of about 15 nucleobases. In some embodiments, a first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobble pairs when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a first domain is fully complementary to a target PNPLA3 transcript. In some embodiments, a first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) sugars with 2'-F modification. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first domain independently comprise a 2'-F modification. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first domain independently comprise a 2'-F modification. In some embodiments, about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in a first domain independently comprise a 2'-F modification. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first domain

comprises 2'-OMe. In some embodiments, about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in a first domain comprises 2'-OMe. In some embodiments, no more than about 50% of sugars in a first domain comprises 2'-OMe. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 50% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first domain comprises 2'-OR. In some embodiments, about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in a first domain comprises 2'-OR, wherein R is not −H. In some embodiments, no more than about 50% of sugars in a first domain comprises 2'-OR. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-MOE modification. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification. In some embodiments, the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-MOE modified sugar. In some embodiments, a first domain comprises a PS internucleotidic linkage and a PN internucleotidic linkage. In some embodiments, each internucleotidic linkage in a first domain is independently a PO internucleotidic linkage, a PS internucleotidic linkage or a PN internucleotidic linkage. In some embodiments, first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 − about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a first domain are modified internucleotidic linkages. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-

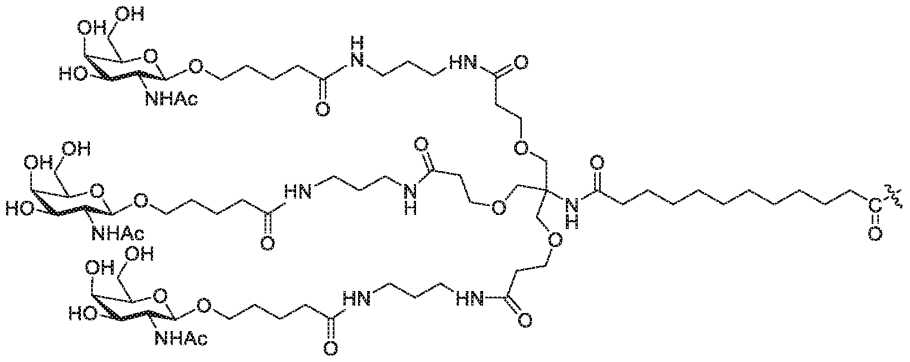
95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a first domain are modified internucleotidic linkages. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage.

[00026] In some embodiments, a first domain comprises one or more phosphorothioate internucleotidic linkages. In some embodiments, a first domain comprises 1, 2, 3, 4, or 5 non-negatively charged internucleotidic linkages. In some embodiments, an internucleotidic linkage between the first and the second nucleosides of a first domain is a non-negatively charged internucleotidic linkage. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a first domain is *Sp*. In some embodiments, an internucleotidic linkage between the first and the second nucleosides of the first domain is *Rp*. In some embodiments, an internucleotidic linkage between the last and the second last nucleosides of the first domain is *Rp*. In some embodiments, each internucleotidic linkage in a first domain is independently a modified internucleotidic linkage. In some embodiments, a first domain can recruit, or promotes or contributes to recruitment of, an ADAR protein to a target PNPLA3 transcript.

[00027] In some embodiments, a second domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a second domain has a length of about 5-15 nucleobases. In some embodiments, a second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a second domain comprises two or more mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a second domain comprises one and no more than one mismatch when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a second domain comprises two and no more than two mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges when the oligonucleotide is aligned with a target PNPLA3 transcript for

complementarity. In some embodiments, each bulge independently comprises one or more base pairs that are not Watson-Crick or wobble pairs. In some embodiments, a second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobble pairs when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, a second domain comprise a nucleoside opposite to a target adenosine when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity. In some embodiments, an opposite nucleobase is optionally substituted or protected U, or is an optionally substituted or protected tautomer of U. In some embodiments, an opposite nucleobase is U. In some embodiments, an oligonucleotide comprises a nucleobase BA, wherein BA is or comprises Ring BA or a tautomer thereof, wherein Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms. In some embodiments, Ring BA has the structure of . In some embodiments, a second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently with a modification that is not 2'-F. In some embodiments, a target adenosine is at a position within the PNPLA3 transcript encoding for an amino acid at position 148 of a PNPLA3 polypeptide. In some embodiments, a target adenosine is at a position within the PNPLA3 transcript encoding for an amino acid at position 148 of SEQ ID NO: 2. In some embodiments, an amino acid is methionine. In some embodiments, a second domain comprises a PS internucleotidic linkage and a PN internucleotidic linkage. In some embodiments, each internucleotidic linkage in a second domain is independently a PO internucleotidic linkage, a PS internucleotidic linkage or a PN internucleotidic linkage. In some embodiments, each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each PS internucleotidic linkage is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a n001 internucleotidic linkage.

[00028] In some embodiments, an oligonucleotide comprises an additional chemical moiety. In some embodiments, an oligonucleotide comprises an asialoglycoprotein receptor ligand. In some embodiments, an oligonucleotide comprises GalNAc. In some embodiments, an oligonucleotide comprises



. In some embodiments, an oligonucleotide is in a pharmaceutically acceptable salt form.

[00029] In some embodiments, the number of chiral linkage phosphorus in the oligonucleotide is about or at least about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30. In some embodiments, each chiral linkage phosphorus independently has a diastereomeric purity of about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, diastereomeric purity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%), and nc is the number of chiral linkage phosphorus in the oligonucleotide. In some embodiments, purity of the oligonucleotide is about 20%-100%, or is about or at least about 20%-95%, 30%-90%, 40%-85%, 40%-80%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, or 90% (e.g., peak area% at 260 nm).

[00030] In some embodiments, the present disclosure provides a pharmaceutical composition which comprises or delivers an effective amount of an oligonucleotide disclosed herein or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. In some embodiments, a composition comprising a plurality of oligonucleotides, wherein each oligonucleotides of the plurality is independently a particular oligonucleotide or a salt thereof, wherein the particular oligonucleotide is an oligonucleotide disclosed herein. In some embodiments, an oligonucleotide composition comprises a plurality of oligonucleotides, wherein oligonucleotides of the plurality share: 1) a common base sequence; and 2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages"); wherein each oligonucleotide of the plurality is independently an oligonucleotide disclosed herein (e.g., in an acid, base, or salt form). In some embodiments, an oligonucleotide composition comprises a plurality of oligonucleotides, wherein oligonucleotides of the plurality share: 1) a common base sequence, and 2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages"); wherein the common base sequence is complementary to a base sequence of a

portion of PNPLA3 transcript which portion comprises a target adenosine. In some embodiments, a common base sequence is complementary to a base sequence of a portion of a PNPLA3 transcript with 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches which are not Watson-Crick base pairs. In some embodiments, a common base sequence is complementary to a base sequence of a portion of a PNPLA3 transcript with 0-5 mismatches which are not Watson-Crick base pairs. In some embodiments, a common base sequence is 100% complementary to a base sequence of a portion of a PNPLA3 transcript across the length of the common base sequence except the nucleoside opposite to a target adenosine. In some embodiments, a common base sequence is 100% complementary to a base sequence of a portion of a PNPLA3 transcript across the length of the common base sequence. In some embodiments, a portion of a PNPLA3 transcript comprises a target adenosine in a codon encoding an amino acid at position 148 of SEQ ID NO: 1 or 2. In some embodiments, a portion of a PNPLA3 transcript comprises a target adenosine in a codon encoding an amino acid at position 148 of SEQ ID NO: 2. In some embodiments, a composition can edit a target A to I when contacted with a PNPLA3 transcript in a system expressing ADAR.

[00031] In some embodiments, oligonucleotides of the plurality share the same base and sugar modifications. In some embodiments, oligonucleotides of the plurality share the same pattern of backbone chiral centers. In some embodiments, a composition is enriched for oligonucleotides of the plurality compared to a stereorandom preparation of the oligonucleotides wherein no internucleotidic linkages are chirally controlled. In some embodiments, a non-random level of all oligonucleotides in a composition that share the common base sequence and the same base and sugar modifications are oligonucleotides of the plurality. In some embodiments, a non-random level of all oligonucleotides in a composition that share the common base sequence are oligonucleotides of the plurality. In some embodiments, oligonucleotides of the plurality are of the same oligonucleotide or one or more pharmaceutically acceptable salts thereof. In some embodiments, oligonucleotides of the plurality are one or more pharmaceutically acceptable salts of the same acid-form oligonucleotide. In some embodiments, oligonucleotides of the plurality are of the same constitution. In some embodiments, a non-random level of all oligonucleotides in the composition that share the same base sequence as oligonucleotides of the plurality are oligonucleotides of the plurality. In some embodiments, a non-random level of all oligonucleotides in the composition that share the same constitution are oligonucleotides of the plurality. In some embodiments, a level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus. In some embodiments, a level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about 20%-100%, or is about or at least about 20%-95%, 30%-90%, 40%-85%, 40%-80%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, or 90%. In some embodiments, oligonucleotides of the plurality are of the same structure. In some embodiments, oligonucleotides of the

plurality are sodium salts. In some embodiments, oligonucleotides of the plurality share the same linkage phosphorus stereochemistry at 10 or more chiral internucleotidic linkages. In some embodiments, oligonucleotides of the plurality share the same linkage phosphorus stereochemistry at each phosphorothioate internucleotidic linkages. In some embodiments, oligonucleotides of the plurality do not share the same linkage phosphorus stereochemistry at one or more or any non-negatively charged internucleotidic linkages.

[00032] In some embodiments, the present disclosure provides a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition disclosed herein. In some embodiments, the present disclosure provides a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising converting the amino acid at position 148 of the PNPLA3 polypeptide into a valine. In some embodiments, the present disclosure provides a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition disclosed herein. In some embodiments, the present disclosure provides a method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in PNPLA3 in the genome of a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in PNPLA3 in the genome of a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide. In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising administering or delivering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or composition disclosed herein.

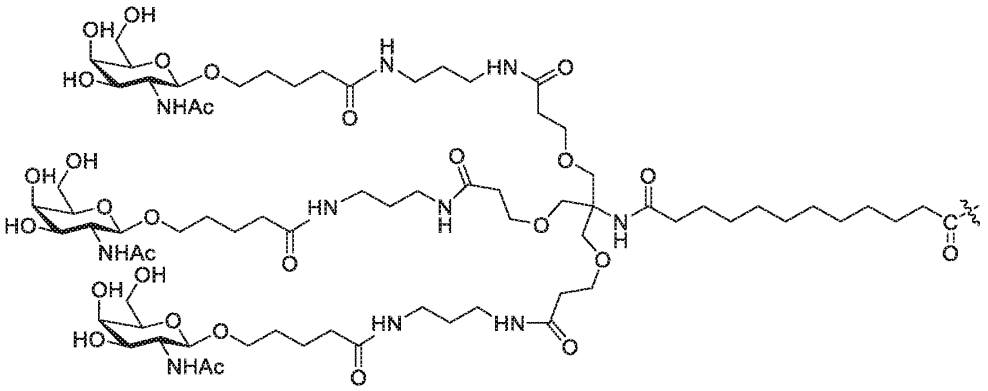
[00033] In some embodiments, a condition, disorder or disease is amenable to an A to G or A to I

modification. In some embodiments, a condition, disease or disorder is associated with a PNPLA3 I148M mutation. In some embodiments, a subject comprises an I148M mutation in PNPLA3. In some embodiments, a subject is homozygous for the mutation. In some embodiments, a subject is heterozygous for the mutation. In some embodiments, a condition, disorder or disease is a liver condition, disorder or disease. In some embodiments, a condition, disorder or disease is a metabolic liver condition, disorder or disease. In some embodiments, a condition, disorder or disease is hepatitis. In some embodiments, a condition, disorder or disease is fibrosis. In some embodiments, a condition, disorder or disease is cirrhosis. In some embodiments, a condition, disorder or disease is HCC. In some embodiments, a condition, disorder or disease is liver failure. In some embodiments, oligonucleotides administered to a subject are GalNAc-conjugated oligonucleotides.

[00034] In some embodiments, the present disclosure provides use of an oligonucleotide or composition disclosed herein for editing a target adenosine in a codon. In some embodiments, sequence, expression, level and/or activity of a protein is altered.

[00035] In some embodiments, the present disclosure provides a method for modulating a protein interaction with an agent in a system wherein a protein is translated from its encoding RNA, comprising administering to the system an oligonucleotide or composition disclosed herein, wherein an adenosine in the encoding RNA is edited, wherein a protein is translated from the edited mRNA ("the edited protein"), wherein the edited protein differs from the unedited protein at an amino acid residue involving in the protein-agent interaction. In some embodiments, an agent is or comprises a small molecule. In some embodiments, an agent is or comprises a lipid. In some embodiments, an agent is or comprises a triglyceride. In some embodiments, a protein is PNPLA3 or a variant thereof. In some embodiments, an oligonucleotide is delivered by administering to the subject an effective amount of a conjugate of the oligonucleotide with an additional chemical moiety or a salt thereof.

[00036] In some embodiments, the present disclosure provides a method for delivering to a system an oligonucleotide, comprising administering to the system a conjugate of the oligonucleotide with an additional chemical moiety or a salt thereof. In some embodiments, a system is or comprises a cell. In some embodiments, a system is or comprises a tissue. In some embodiments, a system is or comprises an organ. In some embodiments, a system is a subject. In some embodiments, a system is a human. In some embodiments, an additional chemical moiety is or comprises a targeting moiety. In some embodiments, an additional chemical moiety is or comprises GalNAc. In some embodiments, an additional chemical moiety is or comprises optionally substituted



. In some embodiments, an additional chemical moiety is directly conjugated to the oligonucleotide. In some embodiments, an additional chemical moiety is conjugated via a linker to oligonucleotide. In some embodiments, a linker is or comprises L001.

[00037] In some embodiments, as demonstrated herein chirally controlled oligonucleotide compositions provide a number of advantages, e.g., higher stability, activities, etc., compared to corresponding stereorandom oligonucleotide compositions. In some embodiments, it was observed that chirally controlled oligonucleotide compositions provide high levels of adenosine modifying (e.g., converting A to I) activities with various isoforms of an ADAR protein (e.g., p150 and p110 forms of ADAR1) while corresponding stereorandom compositions provide high levels of adenosine modifying (e.g., converting A to I) activities with only certain isoforms of an ADAR protein (e.g., p150 isoform of ADAR1).

[00038] In some embodiments, provided oligonucleotides comprise an additional moiety, e.g., a targeting moiety, a carbohydrate moiety, etc. In some embodiments, an additional moiety is or comprises a ligand for an asialoglycoprotein receptor. In some embodiments, an additional moiety is or comprises GalNAc or derivatives thereof. Among other things, additional moieties may facilitate delivery to certain target locations, e.g., cells, tissues, organs, etc. (e.g., locations comprising receptors that interact with additional moieties). In some embodiments, additional moieties facilitate delivery to liver.

[00039] In some embodiments, the present disclosure provides technologies for preparing oligonucleotides and compositions thereof, particularly chirally controlled oligonucleotide compositions. In some embodiments, provided oligonucleotides and compositions thereof are of high purity. In some embodiments, oligonucleotides of the present disclosure are at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% stereochemically pure at linkage phosphorus of chiral internucleotidic linkages. In some embodiments, oligonucleotides of the present disclosure are prepared stereoselectively and are substantially free of stereoisomers. In some embodiments, in provided compositions comprising a plurality of oligonucleotides which share the same base sequence of the same pattern of chiral linkage phosphorus stereochemistry (e.g., comprising one or more of *Rp* and/or *Sp*, wherein each chiral linkage phosphorus is independently *Rp* or *Sp*), at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% of all oligonucleotides in the composition that

share the same base sequence as oligonucleotides of the plurality share the same pattern of chiral linkage phosphorus stereochemistry or are oligonucleotides of the plurality. In some embodiments, in provided compositions comprising a plurality of oligonucleotides which share the same base sequence of the same pattern of chiral linkage phosphorus stereochemistry, at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% of all oligonucleotides in the composition that share the same constitution as oligonucleotides of the plurality share the same pattern of chiral linkage phosphorus stereochemistry or are oligonucleotides of the plurality.

[00040] In some embodiments, the present disclosure describes useful technologies for assessing oligonucleotide and compositions thereof. For example, various technologies of the present disclosure are useful for assessing adenosine modification. As appreciated by those skilled in the art, in some embodiments, modification/editing of adenosine can be assessed through sequencing, mass spectrometry, assessment (e.g., levels, activities, etc.) of products (e.g., RNA, protein, etc.) of modified nucleic acids (e.g., wherein adenosines of target nucleic acids are converted to inosines), etc., optionally in view of other components (e.g., ADAR proteins) presence in modification systems (e.g., an *in vitro* system, an *ex vivo* system, cells, tissues, organs, organisms, subjects, etc.). Those skilled in the art will appreciate that oligonucleotides which provide adenosine modification of a target nucleic acid can also provide modified nucleic acid (e.g., wherein a target adenosine is converted into I) and one or more products thereof (e.g., mRNA, proteins, etc.). Certain useful technologies are described in the Examples.

[00041] As described herein, oligonucleotides and compositions of the present disclosure may be provided/utilized in various forms. In some embodiments, the present disclosure provides compositions comprising one or more forms of oligonucleotides, e.g., acid forms (e.g., in which natural phosphate linkages exist as –O(P(O)(OH)–O–, phosphorothioate internucleotidic linkages exist as –O(P(O)(SH)–O–), base forms, salt forms (e.g., in which natural phosphate linkages exist as salt forms (e.g., sodium salt (–O(P(O)(O^-Na^+)–O–), phosphorothioate internucleotidic linkages exist as salt forms (e.g., sodium salt (–O(P(O)(S^-Na^+)–O–) etc. As appreciated by those skilled in the art, oligonucleotides can exist in various salt forms, including pharmaceutically acceptable salts, and in solutions (e.g., various aqueous buffering system), cations may dissociate from anions. In some embodiments, the present disclosure provides a pharmaceutical composition comprising a provided oligonucleotide and/or one or more pharmaceutically acceptable salts thereof, and a pharmaceutically acceptable carrier. In some embodiments, pharmaceutical compositions are chirally controlled oligonucleotide compositions.

[00042] Provided technologies can be utilized for various purposes. For example, those skilled in the art will appreciate that provided technologies are useful for many purposes involving modification of adenosine, e.g., introduction of A to I variations that may be read as G during translation, modulate levels of certain nucleic acids and/or products encoded thereby (e.g., reducing levels of proteins by introducing A to I modifications), etc.

[00043] In some embodiments, the present disclosure provides technologies for preventing or treating a

condition, disorder or disease that is amenable to an adenosine modification, e.g. conversion of A to I. As appreciated by those skilled in the art, I may perform one or more functions of G, e.g., in base pairing, translation, etc. In some embodiments, conversion of A to I may result in one or more products, e.g., proteins, of the G-version nucleic acid. In some embodiments, the present disclosure provides technologies for preventing or treating a condition, disorder or disease associated with a mutation, comprising administering to a subject susceptible thereto or suffering therefrom a provided oligonucleotide or composition thereof, which oligonucleotide or composition can mediate the effects of the mutation.

[00044] In some embodiments, the present disclosure provides technologies for preventing or treating a condition, disorder or disease associated with a C to G mutation, comprising administering to a subject susceptible thereto or suffering therefrom a provided oligonucleotide or composition thereof, which oligonucleotide or composition can modify an A in the same codon as the C to G mutation. In some embodiments, provided technologies modify an A in a transcript, e.g., RNA transcript to produce an alternative amino acid codon. In some embodiments, an A is converted into an I. In some embodiments, during translation protein synthesis machineries read I as G. In some embodiments, provided technologies modify an A to an I/G form to encodes one or more proteins that have one or more higher desired activities and/or one or more better desired properties compared those encoded by its corresponding A form. In some embodiments, a G form provides higher levels, compared to its corresponding A form, of one or more proteins that have one or more higher desired activities and/or one or more better desired properties. In some embodiments, products encoded by a G form are structurally different (e.g., longer, in some embodiments, full length proteins) from those encoded by its corresponding A form. In some embodiments, a G form provides structurally identical products (e.g., proteins) compared to its corresponding A form.

[00045] In some embodiments, the present disclosure provides technologies for modulating RNA/protein interactions by, e.g., editing target adenosines using oligonucleotides and composition described herein. In some embodiments, the present disclosure provides technologies for modulating levels of RNA and/or products encoded thereby by, e.g., editing a target adenosine. In some embodiments, the present disclosure provides technologies for increasing levels of RNA and/or products (e.g., polypeptides) encoded thereby by, e.g., editing a target adenosine. In some embodiments, a target adenosine is present in a RNA motif, e.g., an AU-rich element (ARE) motif.

[00046] In some embodiments, editing of an adenosine in a RNA modulates level of a RNA. In some embodiments, editing of an adenosine in a RNA modulates level of a product (e.g., a polypeptide) encoded thereby. In some embodiments, editing of an adenosine in a RNA increases level of the RNA. In some embodiments, editing of an adenosine in a RNA increases level of a product (e.g., a polypeptide) encoded thereby. In some embodiments, a RNA is a transcript. In some embodiments, a RNA is mRNA. In some embodiments, an adenosine is in a UTR region. In some embodiments, an adenosine is in a 5'-UTR region. In some embodiments, an adenosine is in a 3'-UTR region. In some embodiments, an adenosine is in a RNA motif. In some embodiments, the present disclosure provides technologies for preventing or treating a

condition, disorder or disease associated with levels of a transcript and/or a product encoded thereby, comprising administering to a subject susceptible thereto or suffering therefrom a provided oligonucleotide or composition thereof, which oligonucleotide or composition can modify a target adenosine in the transcript. In some embodiments, the present disclosure provides technologies for preventing or treating a condition, disorder or disease, comprising administering to a subject susceptible thereto or suffering therefrom a provided oligonucleotide or composition thereof, which oligonucleotide or composition can modify a target adenosine in a RNA thereby modulating (e.g., increasing) levels of a RNA and/or a product encoded thereby. In some embodiments, a RNA is a transcript. In some embodiments, a transcript is a PNPLA3 transcript, e.g., a PNPLA3 mRNA. In some embodiments, a product encoded thereby is a PNPLA3 polypeptide, e.g., a PNPLA3 protein. In some embodiments, a RNA motif is in a PNPLA3 transcript, e.g., in 5' UTR of a PNPLA3 mRNA. In some embodiments, a RNA motif is in a PNPLA3 transcript, e.g., in 3' UTR of a PNPLA3 mRNA.

[00047] As those skilled in the art will appreciate, many conditions, disorders or diseases are associated with mutations that can be modified by provided technologies and can be prevented and/or treated using provided technologies.

BRIEF DESCRIPTION OF THE DRAWINGS

[00048] Figure 1. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary wild-type (WT) human hepatocytes were dosed with 5uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in I148 codon (i.e., AUC) of WT human PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUC). Cells were harvested after 48 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00049] Figure 2. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 10 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 48 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00050] Figure 3. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes

homozygous for M148 mutation were dosed with 0.1 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00051] Figure 4. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.1 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00052] Figure 5. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.01 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00053] Figure 6. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.01 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00054] Figure 7. Various siRNA constructs targeting PNPLA3 were assessed for effects on lipid droplet formation. Primary human hepatocytes were dosed with indicated concentrations of indicated siRNAs. Cells were then treated with 250 uM linoleic acid (LA) lipid and lipid droplet formation was assessed by fluorescent microscopy.

[00055] Figure 8. Provided technologies can provide editing of target transcripts and produce functional protein product. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and

assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 3 uM of indicated oligonucleotides, including a non-targeting control (NTC, ADR-0108273), and an siRNA construct (DSR-0105686). Cells were then treated with 250 uM linoleic acid (LA) lipid and lipid droplet formation was assessed by fluorescent microscopy.

[00056] Figure 9. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with indicated concentration of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00057] Figure 10. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, m1d, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 10 nM (left bar) or 50 nM (right bar) of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00058] Figure 11. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, m1d, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 10 nM (left bar) or 50 nM (right bar) of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00059] Figure 12. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 10 nM (left bar) or 50 nM (right bar) of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of

mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00060] Figure 13. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with indicated concentration of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00061] Figure 14. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with indicated concentration of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00062] Figure 15. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation from two different donors were dosed with indicated concentration of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00063] Figure 16. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 50 nM (left bar) or 10 nM (right bar) of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of

mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

[00064] Figure 17. Provided technologies can provide editing of target transcripts. Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU], [3nT]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar, etc.), and stereochemistry and patterns thereof were designed and assessed. Primary human hepatocytes homozygous for M148 mutation were dosed with 50 nM (left bar) or 10 nM (right bar) of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in a codon that can be read as a valine codon (i.e., GUG). Cells were harvested after 72 hours and RNA was collected and reverse-transcribed into cDNA. Editing was quantified by Sanger sequencing.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

[00065] Technologies of the present disclosure may be understood more readily by reference to the following detailed description of certain embodiments.

Definitions

[00066] As used herein, the following definitions shall apply unless otherwise indicated. For purposes of this disclosure, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 75th Ed. Additionally, general principles of organic chemistry are described in "Organic Chemistry", Thomas Sorrell, University Science Books, Sausalito: 1999, and "March's Advanced Organic Chemistry", 5th Ed., Ed.: Smith, M.B. and March, J., John Wiley & Sons, New York: 2001.

[00067] As used herein in the present disclosure, unless otherwise clear from context, (i) the term "a" or "an" may be understood to mean "at least one"; (ii) the term "or" may be understood to mean "and/or"; (iii) the terms "comprising", "comprise", "including" (whether used with "not limited to" or not), and "include" (whether used with "not limited to" or not) may be understood to encompass itemized components or steps whether presented by themselves or together with one or more additional components or steps; (iv) the term "another" may be understood to mean at least an additional/second one or more; (v) the terms "about" and "approximately" may be understood to permit standard variation as would be understood by those of ordinary skill in the art; and (vi) where ranges are provided, endpoints are included.

[00068] Unless otherwise specified, description of oligonucleotides and elements thereof (e.g., base sequence, sugar modifications, internucleotidic linkages, linkage phosphorus stereochemistry, patterns thereof, etc.) is from 5' to 3'. As those skilled in the art will appreciate, in some embodiments, oligonucleotides may be provided and/or utilized as salt forms, particularly pharmaceutically acceptable salt forms, e.g., sodium salts. As those skilled in the art will also appreciate, in some embodiments, individual oligonucleotides within

a composition may be considered to be of the same constitution and/or structure even though, within such composition (e.g., a liquid composition), particular such oligonucleotides might be in different salt form(s) (and may be dissolved and the oligonucleotide chain may exist as an anion form when, e.g., in a liquid composition) at a particular moment in time. For example, those skilled in the art will appreciate that, at a given pH, individual internucleotidic linkages along an oligonucleotide chain may be in an acid (H) form, or in one of a plurality of possible salt forms (e.g., a sodium salt, or a salt of a different cation, depending on which ions might be present in the preparation or composition), and will understand that, so long as their acid forms (e.g., replacing all cations, if any, with H^+) are of the same constitution and/or structure, such individual oligonucleotides may properly be considered to be of the same constitution and/or structure.

[00069] Aliphatic: As used herein, "aliphatic" means a straight-chain (i.e., unbranched) or branched, substituted or unsubstituted hydrocarbon chain that is completely saturated or that contains one or more units of unsaturation (but not aromatic), or a substituted or unsubstituted monocyclic, bicyclic, or polycyclic hydrocarbon ring that is completely saturated or that contains one or more units of unsaturation (but not aromatic), or combinations thereof. In some embodiments, aliphatic groups contain 1-50 aliphatic carbon atoms. In some embodiments, aliphatic groups contain 1-20 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-10 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-9 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-8 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-7 aliphatic carbon atoms. In other embodiments, aliphatic groups contain 1-6 aliphatic carbon atoms. In still other embodiments, aliphatic groups contain 1-5 aliphatic carbon atoms, and in yet other embodiments, aliphatic groups contain 1, 2, 3, or 4 aliphatic carbon atoms. Suitable aliphatic groups include, but are not limited to, linear or branched, substituted or unsubstituted alkyl, alkenyl, alkynyl groups and hybrids thereof such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl or (cycloalkyl)alkenyl.

[00070] Alkenyl: As used herein, the term "alkenyl" refers to an aliphatic group, as defined herein, having one or more double bonds.

[00071] Alkyl: As used herein, the term "alkyl" is given its ordinary meaning in the art and may include saturated aliphatic groups, including straight-chain alkyl groups, branched-chain alkyl groups, cycloalkyl (alicyclic) groups, alkyl substituted cycloalkyl groups, and cycloalkyl substituted alkyl groups. In some embodiments, alkyl has 1-100 carbon atoms. In certain embodiments, a straight chain or branched chain alkyl has about 1-20 carbon atoms in its backbone (e.g., C_1-C_{20} for straight chain, C_2-C_{20} for branched chain), and alternatively, about 1-10. In some embodiments, cycloalkyl rings have from about 3-10 carbon atoms in their ring structure where such rings are monocyclic, bicyclic, or polycyclic, and alternatively about 5, 6 or 7 carbons in the ring structure. In some embodiments, an alkyl group may be a lower alkyl group, wherein a lower alkyl group comprises 1-4 carbon atoms (e.g., C_1-C_4 for straight chain lower alkyls).

[00072] Alkynyl: As used herein, the term "alkynyl" refers to an aliphatic group, as defined herein, having one or more triple bonds.

[00073] Analog: The term "analog" includes any chemical moiety which differs structurally from a

reference chemical moiety or class of moieties, but which is capable of performing at least one function of such a reference chemical moiety or class of moieties. As non-limiting examples, a nucleotide analog differs structurally from a nucleotide but performs at least one function of a nucleotide; a nucleobase analog differs structurally from a nucleobase but performs at least one function of a nucleobase; etc.

[00074] Animal: As used herein, the term "animal" refers to any member of the animal kingdom. In some embodiments, "animal" refers to humans, at any stage of development. In some embodiments, "animal" refers to non-human animals, at any stage of development. In certain embodiments, the non-human animal is a mammal (e.g., a rodent, a mouse, a rat, a rabbit, a monkey, a dog, a cat, a sheep, cattle, a primate and/or a pig). In some embodiments, animals include, but are not limited to, mammals, birds, reptiles, amphibians, fish and/or worms. In some embodiments, an animal may be a transgenic animal, a genetically-engineered animal and/or a clone.

[00075] Aryl: The term "aryl", as used herein, used alone or as part of a larger moiety as in "aralkyl," "aralkoxy," or "aryloxyalkyl," refers to monocyclic, bicyclic or polycyclic ring systems having a total of five to thirty ring members, wherein at least one ring in the system is aromatic. In some embodiments, an aryl group is a monocyclic, bicyclic or polycyclic ring system having a total of five to fourteen ring members, wherein at least one ring in the system is aromatic, and wherein each ring in the system contains 3 to 7 ring members. In some embodiments, each monocyclic ring unit is aromatic. In some embodiments, an aryl group is a biaryl group. The term "aryl" may be used interchangeably with the term "aryl ring." In certain embodiments of the present disclosure, "aryl" refers to an aromatic ring system which includes, but is not limited to, phenyl, biphenyl, naphthyl, binaphthyl, anthracyl and the like, which may bear one or more substituents. Also included within the scope of the term "aryl," as it is used herein, is a group in which an aromatic ring is fused to one or more non–aromatic rings, such as indanyl, phthalimidyl, naphthimidyl, phenanthridinyl, or tetrahydronaphthyl, and the like.

[00076] Characteristic portion: As used herein, the term "characteristic portion", in the broadest sense, refers to a portion of a substance whose presence (or absence) correlates with presence (or absence) of a particular feature, attribute, or activity of the substance. In some embodiments, a characteristic portion of a substance is a portion that is found in the substance and in related substances that share the particular feature, attribute or activity, but not in those that do not share the particular feature, attribute or activity. In certain embodiments, a characteristic portion shares at least one functional characteristic with the intact substance. For example, in some embodiments, a "characteristic portion" of a protein or polypeptide is one that contains a continuous stretch of amino acids, or a collection of continuous stretches of amino acids, that together are characteristic of a protein or polypeptide. In some embodiments, each such continuous stretch generally contains at least 2, 5, 10, 15, 20, 50, or more amino acids. In general, a characteristic portion of a substance (*e.g.*, of a protein, antibody, *etc.*) is one that, in addition to the sequence and/or structural identity specified above, shares at least one functional characteristic with the relevant intact substance. In some embodiments, a characteristic portion may be biologically active.

[00077] Chiral control: As used herein, "chiral control" refers to control of the stereochemical designation of the chiral linkage phosphorus in a chiral internucleotidic linkage within an oligonucleotide. As used herein, a chiral internucleotidic linkage is an internucleotidic linkage whose linkage phosphorus is chiral. In some embodiments, a control is achieved through a chiral element that is absent from the sugar and base moieties of an oligonucleotide, for example, in some embodiments, a control is achieved through use of one or more chiral auxiliaries during oligonucleotide preparation, which chiral auxiliaries often are part of chiral phosphoramidites used during oligonucleotide preparation. In contrast to chiral control, a person having ordinary skill in the art will appreciate that conventional oligonucleotide synthesis which does not use chiral auxiliaries cannot control stereochemistry at a chiral internucleotidic linkage if such conventional oligonucleotide synthesis is used to form the chiral internucleotidic linkage. In some embodiments, the stereochemical designation of each chiral linkage phosphorus in each chiral internucleotidic linkage within an oligonucleotide is controlled.

[00078] Chirally controlled oligonucleotide composition: The terms "chirally controlled oligonucleotide composition", "chirally controlled nucleic acid composition", and the like, as used herein, refers to a composition that comprises a plurality of oligonucleotides (or nucleic acids) which share a common base sequence, wherein the plurality of oligonucleotides (or nucleic acids) share the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled or stereodefined internucleotidic linkages, whose chiral linkage phosphorus is Rp or Sp in the composition ("stereodefined"), not a random Rp and Sp mixture as non-chirally controlled internucleotidic linkages). In some embodiments, a chirally controlled oligonucleotide composition comprises a plurality of oligonucleotides (or nucleic acids) that share: 1) a common base sequence, 2) a common pattern of backbone linkages, and 3) a common pattern of backbone phosphorus modifications, wherein the plurality of oligonucleotides (or nucleic acids) share the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled or stereodefined internucleotidic linkages, whose chiral linkage phosphorus is Rp or Sp in the composition ("stereodefined"), not a random Rp and Sp mixture as non-chirally controlled internucleotidic linkages). Level of the plurality of oligonucleotides (or nucleic acids) in a chirally controlled oligonucleotide composition is pre-determined/controlled or enriched (e.g., through chirally controlled oligonucleotide preparation to stereoselectively form one or more chiral internucleotidic linkages) compared to a random level in a non-chirally controlled oligonucleotide composition. In some embodiments, about 1%-100%, (e.g., about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, or about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) of all oligonucleotides in a chirally controlled oligonucleotide composition are oligonucleotides of the plurality. In some embodiments, about 1%-100%, (e.g., about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, or about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%,

85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) of all oligonucleotides in a chirally controlled oligonucleotide composition that share the common base sequence, the common pattern of backbone linkages, and the common pattern of backbone phosphorus modifications are oligonucleotides of the plurality. In some embodiments, a level is about 1%-100%, (e.g., about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, or about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) of all oligonucleotides in a composition, or of all oligonucleotides in a composition that share a common base sequence (e.g., of a plurality of oligonucleotide or an oligonucleotide type), or of all oligonucleotides in a composition that share a common base sequence, a common pattern of backbone linkages, and a common pattern of backbone phosphorus modifications, or of all oligonucleotides in a composition that share a common base sequence, a common patter of base modifications, a common pattern of sugar modifications, a common pattern of internucleotidic linkage types, and/or a common pattern of internucleotidic linkage modifications. In some embodiments, the plurality of oligonucleotides share the same stereochemistry at about 1-50 (e.g., about 1-10, 1-20, 5-10, 5-20, 10-15, 10-20, 10-25, 10-30, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, or at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) chiral internucleotidic linkages. In some embodiments, the plurality of oligonucleotides share the same stereochemistry at about 1%-100% (e.g., about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99%) of chiral internucleotidic linkages. In some embodiments, oligonucleotides (or nucleic acids) of a plurality share the same pattern of sugar and/or nucleobase modifications, in any. In some embodiments, oligonucleotides (or nucleic acids) of a plurality are various forms of the same oligonucleotide (e.g., acid and/or various salts of the same oligonucleotide). In some embodiments, oligonucleotides (or nucleic acids) of a plurality are of the same constitution. In some embodiments, level of the oligonucleotides (or nucleic acids) of the plurality is about 1%-100%, (e.g., about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, or about 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%, or at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%) of all oligonucleotides (or nucleic acids) in a composition that share the same constitution as the oligonucleotides (or nucleic acids) of the plurality. In some embodiments, each chiral internucleotidic linkage is a chiral controlled internucleotidic linkage, and the composition is a completely chirally controlled oligonucleotide composition. In some embodiments, oligonucleotides (or nucleic acids) of a plurality are structurally identical. In some

embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%, typically at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%. In some embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 95%. In some embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 96%. In some embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 97%. In some embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 98%. In some embodiments, a chirally controlled internucleotidic linkage has a diastereopurity of at least 99%. In some embodiments, a percentage of a level is or is at least $(DS)^{nc}$, wherein DS is a diastereopurity as described in the present disclosure (e.g., 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus as described in the present disclosure (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 5-50, 5-40, 5-30, 5-25, 5-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more). In some embodiments, a percentage of a level is or is at least $(DS)^{nc}$, wherein DS is a diastereopurity as described in the present disclosure (e.g., 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chirally controlled internucleotidic linkages as described in the present disclosure (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 5-50, 5-40, 5-30, 5-25, 5-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more). In some embodiments, a percentage of a level is or is at least $(DS)^{nc}$, wherein DS is 95%-100%. For example, when DS is 99% and nc is 10, the percentage is or is at least 90% ($(99\%)^{10} \approx 0.90 = 90\%$). In some embodiments, level of a plurality of oligonucleotides in a composition is represented as the product of the diastereopurity of each chiral linkage phosphorus. In some embodiments, level of a plurality of oligonucleotides in a composition is represented as the product of the diastereopurity of each chirally controlled internucleotidic linkage in the oligonucleotides. In some embodiments, diastereopurity of an internucleotidic linkage connecting two nucleosides in an oligonucleotide (or nucleic acid) is represented by the diastereopurity of an internucleotidic linkage of a dimer connecting the same two nucleosides, wherein the dimer is prepared using comparable conditions, in some instances, identical synthetic cycle conditions (e.g., for the linkage between Nx and Ny in an oligonucleotide ….NxNy….., the dimer is NxNy). In some embodiments, not all chiral internucleotidic linkages are chiral controlled internucleotidic linkages, and the composition is a partially chirally controlled oligonucleotide composition. In some embodiments, a non-chirally controlled internucleotidic linkage has a diastereopurity of less than about 80%, 75%, 70%, 65%, 60%, 55%, or of about 50%, as typically observed in stereorandom oligonucleotide compositions (e.g., as appreciated by those skilled in the art, from traditional oligonucleotide synthesis, e.g., the phosphoramidite method). In some embodiments, oligonucleotides (or nucleic acids) of a plurality are of the same type. In some embodiments, a chirally controlled oligonucleotide composition comprises non-random or controlled levels of individual oligonucleotide or nucleic acids types. For instance, in some embodiments a chirally controlled oligonucleotide composition comprises one and no more than one oligonucleotide type. In some embodiments,

a chirally controlled oligonucleotide composition comprises more than one oligonucleotide type. In some embodiments, a chirally controlled oligonucleotide composition comprises multiple oligonucleotide types. In some embodiments, a chirally controlled oligonucleotide composition is a composition of oligonucleotides of an oligonucleotide type, which composition comprises a non-random or controlled level of a plurality of oligonucleotides of the oligonucleotide type.

[00079] Comparable: The term "comparable" is used herein to describe two (or more) sets of conditions or circumstances that are sufficiently similar to one another to permit comparison of results obtained or phenomena observed. In some embodiments, comparable sets of conditions or circumstances are characterized by a plurality of substantially identical features and one or a small number of varied features. Those of ordinary skill in the art will appreciate that sets of conditions are comparable to one another when characterized by a sufficient number and type of substantially identical features to warrant a reasonable conclusion that differences in results obtained or phenomena observed under the different sets of conditions or circumstances are caused by or indicative of the variation in those features that are varied.

[00080] Cycloaliphatic: The term "cycloaliphatic," "carbocycle," "carbocyclyl," "carbocyclic radical," and "carbocyclic ring," are used interchangeably, and as used herein, refer to saturated or partially unsaturated, but non-aromatic, cyclic aliphatic monocyclic, bicyclic, or polycyclic ring systems, as described herein, having, unless otherwise specified, from 3 to 30 ring members. Cycloaliphatic groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl, cyclooctenyl, norbornyl, adamantyl, and cyclooctadienyl. In some embodiments, a cycloaliphatic group has 3–6 carbons. In some embodiments, a cycloaliphatic group is saturated and is cycloalkyl. The term "cycloaliphatic" may also include aliphatic rings that are fused to one or more aromatic or nonaromatic rings, such as decahydronaphthyl or tetrahydronaphthyl. In some embodiments, a cycloaliphatic group is bicyclic. In some embodiments, a cycloaliphatic group is tricyclic. In some embodiments, a cycloaliphatic group is polycyclic. In some embodiments, "cycloaliphatic" refers to C_3-C_6 monocyclic hydrocarbon, or C_8-C_{10} bicyclic or polycyclic hydrocarbon, that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic, that has a single point of attachment to the rest of the molecule, or a C_9-C_{16} polycyclic hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic, that has a single point of attachment to the rest of the molecule.

[00081] Heteroaliphatic: The term "heteroaliphatic", as used herein, is given its ordinary meaning in the art and refers to aliphatic groups as described herein in which one or more carbon atoms are independently replaced with one or more heteroatoms (e.g., oxygen, nitrogen, sulfur, silicon, phosphorus, and the like). In some embodiments, one or more units selected from C, CH, CH_2, and CH_3 are independently replaced by one or more heteroatoms (including oxidized and/or substituted forms thereof). In some embodiments, a heteroaliphatic group is heteroalkyl. In some embodiments, a heteroaliphatic group is heteroalkenyl.

[00082] Heteroalkyl: The term "heteroalkyl", as used herein, is given its ordinary meaning in the art and refers to alkyl groups as described herein in which one or more carbon atoms are independently replaced with

one or more heteroatoms (e.g., oxygen, nitrogen, sulfur, silicon, phosphorus, and the like). Examples of heteroalkyl groups include, but are not limited to, alkoxy, poly(ethylene glycol)-, alkyl-substituted amino, tetrahydrofuranyl, piperidinyl, morpholinyl, etc.

[00083] Heteroaryl: The terms "heteroaryl" and "heteroar–", as used herein, used alone or as part of a larger moiety, e.g., "heteroaralkyl," or "heteroaralkoxy," refer to monocyclic, bicyclic or polycyclic ring systems having a total of five to thirty ring members, wherein at least one ring in the system is aromatic and at least one aromatic ring atom is a heteroatom. In some embodiments, a heteroaryl group is a group having 5 to 10 ring atoms (i.e., monocyclic, bicyclic or polycyclic), in some embodiments 5, 6, 9, or 10 ring atoms. In some embodiments, each monocyclic ring unit is aromatic. In some embodiments, a heteroaryl group has 6, 10, or 14 π electrons shared in a cyclic array; and having, in addition to carbon atoms, from one to five heteroatoms. Heteroaryl groups include, without limitation, thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, purinyl, naphthyridinyl, and pteridinyl. In some embodiments, a heteroaryl is a heterobiaryl group, such as bipyridyl and the like. The terms "heteroaryl" and "heteroar–", as used herein, also include groups in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocyclyl rings, where the radical or point of attachment is on the heteroaromatic ring. Non-limiting examples include indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 4H–quinolizinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, and pyrido[2,3–b]–1,4–oxazin–3(4H)–one. A heteroaryl group may be monocyclic, bicyclic or polycyclic. The term "heteroaryl" may be used interchangeably with the terms "heteroaryl ring," "heteroaryl group," or "heteroaromatic," any of which terms include rings that are optionally substituted. The term "heteroaralkyl" refers to an alkyl group substituted by a heteroaryl group, wherein the alkyl and heteroaryl portions independently are optionally substituted.

[00084] Heteroatom: The term "heteroatom", as used herein, means an atom that is not carbon or hydrogen. In some embodiments, a heteroatom is boron, oxygen, sulfur, nitrogen, phosphorus, or silicon (including oxidized forms of nitrogen, sulfur, phosphorus, or silicon; charged forms of nitrogen (e.g., quaternized forms, forms as in iminium groups, etc.), phosphorus, sulfur, oxygen; etc.). In some embodiments, a heteroatom is silicon, phosphorus, oxygen, sulfur or nitrogen. In some embodiments, a heteroatom is silicon, oxygen, sulfur or nitrogen. In some embodiments, a heteroatom is oxygen, sulfur or nitrogen.

[00085] Heterocycle: As used herein, the terms "heterocycle," "heterocyclyl," "heterocyclic radical," and "heterocyclic ring", as used herein, are used interchangeably and refer to a monocyclic, bicyclic or polycyclic ring moiety (e.g., 3-30 membered) that is saturated or partially unsaturated and has one or more heteroatom ring atoms. In some embodiments, a heterocyclyl group is a stable 5– to 7–membered monocyclic or 7– to 10–membered bicyclic heterocyclic moiety that is either saturated or partially unsaturated, and having, in addition to carbon atoms, one or more, preferably one to four, heteroatoms, as defined above. When used in reference

to a ring atom of a heterocycle, the term "nitrogen" includes substituted nitrogen. As an example, in a saturated or partially unsaturated ring having 0–3 heteroatoms selected from oxygen, sulfur and nitrogen, the nitrogen may be N (as in 3,4–dihydro–2H–pyrrolyl), NH (as in pyrrolidinyl), or $^{+}$NR (as in N–substituted pyrrolidinyl). A heterocyclic ring can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Examples of such saturated or partially unsaturated heterocyclic radicals include, without limitation, tetrahydrofuranyl, tetrahydrothienyl, pyrrolidinyl, piperidinyl, pyrrolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, decahydroquinolinyl, oxazolidinyl, piperazinyl, dioxanyl, dioxolanyl, diazepinyl, oxazepinyl, thiazepinyl, morpholinyl, and quinuclidinyl. The terms "heterocycle," "heterocyclyl," "heterocyclyl ring," "heterocyclic group," "heterocyclic moiety," and "heterocyclic radical," are used interchangeably herein, and also include groups in which a heterocyclyl ring is fused to one or more aryl, heteroaryl, or cycloaliphatic rings, such as indolinyl, 3H–indolyl, chromanyl, phenanthridinyl, or tetrahydroquinolinyl. A heterocyclyl group may be monocyclic, bicyclic or polycyclic. The term "heterocyclylalkyl" refers to an alkyl group substituted by a heterocyclyl, wherein the alkyl and heterocyclyl portions independently are optionally substituted.

[00086] Identity: As used herein, the term "identity" refers to the overall relatedness between polymeric molecules, e.g., between nucleic acid molecules (e.g., oligonucleotides, DNA, RNA, etc.) and/or between polypeptide molecules. In some embodiments, polymeric molecules are considered to be "substantially identical" to one another if their sequences are at least 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical. Calculation of the percent identity of two nucleic acid or polypeptide sequences, for example, can be performed by aligning the two sequences for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second sequences for optimal alignment and non-identical sequences can be disregarded for comparison purposes). In certain embodiments, the length of a sequence aligned for comparison purposes is at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or substantially 100% of the length of a reference sequence. The nucleotides at corresponding positions are then compared. When a position in the first sequence is occupied by the same residue (e.g., nucleotide or amino acid) as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which needs to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. For example, the percent identity between two nucleotide sequences can be determined using the algorithm of Meyers and Miller (CABIOS, 1989, 4: 11-17), which has been incorporated into the ALIGN program (version 2.0). In some exemplary embodiments, nucleic acid sequence comparisons made with the ALIGN program use a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The percent identity between two nucleotide sequences can, alternatively, be determined using the GAP program in the GCG software package using an NWSgapdna.CMP matrix.

[00087] Internucleotidic linkage: As used herein, the phrase "internucleotidic linkage" refers generally to a linkage linking nucleoside units of an oligonucleotide or a nucleic acid. In some embodiments, an internucleotidic linkage is a phosphodiester linkage, as extensively found in naturally occurring DNA and RNA molecules (natural phosphate linkage (−OP(=O)(OH)O−), which as appreciated by those skilled in the art may exist as a salt form). In some embodiments, an internucleotidic linkage is a modified internucleotidic linkage (not a natural phosphate linkage). In some embodiments, an internucleotidic linkage is a "modified internucleotidic linkage" wherein at least one oxygen atom or −OH of a phosphodiester linkage is replaced by a different organic or inorganic moiety. In some embodiments, such an organic or inorganic moiety is selected from =S, =Se, =NR', –SR', –SeR', –$N(R')_2$, $B(R')_3$, –S–, –Se–, and –N(R')–, wherein each R' is independently as defined and described in the present disclosure. In some embodiments, an internucleotidic linkage is a phosphotriester linkage, phosphorothioate linkage (or phosphorothioate diester linkage, −OP(=O)(SH)O−, which as appreciated by those skilled in the art may exist as a salt form), or phosphorothioate triester linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate linkage. In some embodiments, an internucleotidic linkage is one of, e.g., PNA (peptide nucleic acid) or PMO (phosphorodiamidate Morpholino oligomer) linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral internucleotidic linkage (e.g., n001 in certain provided oligonucleotides). It is understood by a person of ordinary skill in the art that an internucleotidic linkage may exist as an anion or cation at a given pH due to the existence of acid or base moieties in the linkage. In some embodiments, a modified internucleotidic linkages is a modified internucleotidic linkages designated as s, s1, s2, s3, s4, s5, s6, s7, s8, s9, s10, s11, s12, s13, s14, s15, s16, s17 and s18 as described in WO 2017/210647.

[00088] In vitro: As used herein, the term "in vitro" refers to events that occur in an artificial environment, e.g., in a test tube or reaction vessel, in cell culture, etc., rather than within an organism (e.g., animal, plant and/or microbe).

[00089] In vivo: As used herein, the term "in vivo" refers to events that occur within an organism (e.g., animal, plant and/or microbe).

[00090] Linkage phosphorus: as defined herein, the phrase "linkage phosphorus" is used to indicate that the particular phosphorus atom being referred to is the phosphorus atom present in the internucleotidic linkage, which phosphorus atom corresponds to the phosphorus atom of a phosphodiester internucleotidic linkage as occurs in naturally occurring DNA and RNA. In some embodiments, a linkage phosphorus atom is in a modified internucleotidic linkage, wherein each oxygen atom of a phosphodiester linkage is optionally and independently replaced by an organic or inorganic moiety. In some embodiments, a linkage phosphorus atom is chiral (e.g., as in phosphorothioate internucleotidic linkages). In some embodiments, a linkage phosphorus atom is achiral (e.g., as in natural phosphate linkages).

[00091] Modified nucleobase: The terms "modified nucleobase", "modified base" and the like refer to a chemical moiety which is chemically distinct from a nucleobase, but which is capable of performing at least

one function of a nucleobase. In some embodiments, a modified nucleobase is a nucleobase which comprises a modification. In some embodiments, a modified nucleobase is capable of at least one function of a nucleobase, e.g., forming a moiety in a polymer capable of base-pairing to a nucleic acid comprising an at least complementary sequence of bases. In some embodiments, a modified nucleobase is substituted A, T, C, G, or U, or a substituted tautomer of A, T, C, G, or U. In some embodiments, a modified nucleobase in the context of oligonucleotides refer to a nucleobase that is not A, T, C, G or U.

[00092] Modified nucleoside: The term "modified nucleoside" refers to a moiety derived from or chemically similar to a natural nucleoside, but which comprises a chemical modification which differentiates it from a natural nucleoside. Non-limiting examples of modified nucleosides include those which comprise a modification at the base and/or the sugar. Non-limiting examples of modified nucleosides include those with a 2' modification at a sugar. Non-limiting examples of modified nucleosides also include abasic nucleosides (which lack a nucleobase). In some embodiments, a modified nucleoside is capable of at least one function of a nucleoside, e.g., forming a moiety in a polymer capable of base-pairing to a nucleic acid comprising an at least complementary sequence of bases.

[00093] Modified nucleotide: The term "modified nucleotide" includes any chemical moiety which differs structurally from a natural nucleotide but is capable of performing at least one function of a natural nucleotide. In some embodiments, a modified nucleotide comprises a modification at a sugar, base and/or internucleotidic linkage. In some embodiments, a modified nucleotide comprises a modified sugar, modified nucleobase and/or modified internucleotidic linkage. In some embodiments, a modified nucleotide is capable of at least one function of a nucleotide, e.g., forming a subunit in a polymer capable of base-pairing to a nucleic acid comprising an at least complementary sequence of bases.

[00094] *Modified sugar*: The term "modified sugar" refers to a moiety that can replace a sugar. A modified sugar mimics the spatial arrangement, electronic properties, or some other physicochemical property of a sugar. In some embodiments, as described in the present disclosure, a modified sugar is substituted ribose or deoxyribose. In some embodiments, a modified sugar comprises a 2'-modification. Examples of useful 2'-modification are widely utilized in the art and described herein. In some embodiments, a 2'-modification is 2'-F. In some embodiments, a 2'-modification is 2'-OR, wherein R is optionally substituted C_{1-10} aliphatic. In some embodiments, a 2'-modification is 2'-OMe. In some embodiments, a 2'-modification is 2'-MOE. In some embodiments, a modified sugar is a bicyclic sugar (e.g., a sugar used in LNA, BNA, etc.). In some embodiments, in the context of oligonucleotides, a modified sugar is a sugar that is not ribose or deoxyribose as typically found in natural RNA or DNA.

[00095] Nucleic acid: The term "nucleic acid", as used herein, includes any nucleotides and polymers thereof. The term "polynucleotide", as used herein, refers to a polymeric form of nucleotides of any length, either ribonucleotides (RNA) or deoxyribonucleotides (DNA) or a combination thereof. These terms refer to the primary structure of the molecules and, thus, include double- and single-stranded DNA, and double- and single-stranded RNA. These terms include, as equivalents, analogs of either RNA or DNA comprising

modified nucleotides and/or modified polynucleotides, such as, though not limited to, methylated, protected and/or capped nucleotides or polynucleotides. The terms encompass poly- or oligo-ribonucleotides (RNA) and poly- or oligo-deoxyribonucleotides (DNA); RNA or DNA derived from N-glycosides or C-glycosides of nucleobases and/or modified nucleobases; nucleic acids derived from sugars and/or modified sugars; and nucleic acids derived from phosphate bridges and/or modified internucleotidic linkages. The term encompasses nucleic acids containing any combinations of nucleobases, modified nucleobases, sugars, modified sugars, phosphate bridges or modified internucleotidic linkages. Examples include, and are not limited to, nucleic acids containing ribose moieties, nucleic acids containing deoxy-ribose moieties, nucleic acids containing both ribose and deoxyribose moieties, nucleic acids containing ribose and modified ribose moieties. Unless otherwise specified, the prefix poly- refers to a nucleic acid containing 2 to about 10,000 nucleotide monomer units and wherein the prefix oligo- refers to a nucleic acid containing 2 to about 200 nucleotide monomer units.

[00096] Nucleobase: The term "nucleobase" refers to the parts of nucleic acids that are involved in the hydrogen-bonding that binds one nucleic acid strand to another complementary strand in a sequence specific manner. The most common naturally-occurring nucleobases are adenine (A), guanine (G), uracil (U), cytosine (C), and thymine (T). In some embodiments, a naturally-occurring nucleobases are modified adenine, guanine, uracil, cytosine, or thymine. In some embodiments, a naturally-occurring nucleobases are methylated adenine, guanine, uracil, cytosine, or thymine. In some embodiments, a nucleobase comprises a heteroaryl ring wherein a ring atom is nitrogen, and when in a nucleoside, the nitrogen is bonded to a sugar moiety. In some embodiments, a nucleobase comprises a heterocyclic ring wherein a ring atom is nitrogen, and when in a nucleoside, the nitrogen is bonded to a sugar moiety. In some embodiments, a nucleobase is a "modified nucleobase," a nucleobase other than adenine (A), guanine (G), uracil (U), cytosine (C), and thymine (T). In some embodiments, a modified nucleobase is substituted A, T, C, G or U. In some embodiments, a modified nucleobase is a substituted tautomer of A, T, C, G, or U. In some embodiments, a modified nucleobases is methylated adenine, guanine, uracil, cytosine, or thymine. In some embodiments, a modified nucleobase mimics the spatial arrangement, electronic properties, or some other physicochemical property of the nucleobase and retains the property of hydrogen-bonding that binds one nucleic acid strand to another in a sequence specific manner. In some embodiments, a modified nucleobase can pair with all of the five naturally occurring bases (uracil, thymine, adenine, cytosine, or guanine) without substantially affecting the melting behavior, recognition by intracellular enzymes or activity of the oligonucleotide duplex. As used herein, the term "nucleobase" also encompasses structural analogs used in lieu of natural or naturally-occurring nucleotides, such as modified nucleobases and nucleobase analogs. In some embodiments, a nucleobase is optionally substituted A, T, C, G, or U, or an optionally substituted tautomer of A, T, C, G, or U. In some embodiments, a "nucleobase" refers to a nucleobase unit in an oligonucleotide or a nucleic acid (e.g., A, T, C, G or U as in an oligonucleotide or a nucleic acid).

[00097] Nucleoside: The term "nucleoside" refers to a moiety wherein a nucleobase or a modified

nucleobase is covalently bound to a sugar or a modified sugar. In some embodiments, a nucleoside is a natural nucleoside, e.g., adenosine, deoxyadenosine, guanosine, deoxyguanosine, thymidine, uridine, cytidine, or deoxycytidine. In some embodiments, a nucleoside is a modified nucleoside, e.g., a substituted natural nucleoside selected from adenosine, deoxyadenosine, guanosine, deoxyguanosine, thymidine, uridine, cytidine, and deoxycytidine. In some embodiments, a nucleoside is a modified nucleoside, e.g., a substituted tautomer of a natural nucleoside selected from adenosine, deoxyadenosine, guanosine, deoxyguanosine, thymidine, uridine, cytidine, and deoxycytidine. In some embodiments, a "nucleoside" refers to a nucleoside unit in an oligonucleotide or a nucleic acid.

[00098] Nucleotide: The term "nucleotide" as used herein refers to a monomeric unit of a polynucleotide that consists of a nucleobase, a sugar, and one or more internucleotidic linkages (e.g., phosphate linkages in natural DNA and RNA). The naturally occurring bases [guanine, (G), adenine, (A), cytosine, (C), thymine, (T), and uracil (U)] are derivatives of purine or pyrimidine, though it should be understood that naturally and non-naturally occurring base analogs are also included. The naturally occurring sugar is the pentose (five-carbon sugar) deoxyribose (which forms DNA) or ribose (which forms RNA), though it should be understood that naturally and non-naturally occurring sugar analogs are also included. Nucleotides are linked via internucleotidic linkages to form nucleic acids, or polynucleotides. Many internucleotidic linkages are known in the art (such as, though not limited to, phosphate, phosphorothioates, boranophosphates and the like). Artificial nucleic acids include PNAs (peptide nucleic acids), phosphotriesters, phosphorothionates, H-phosphonates, phosphoramidates, boranophosphates, methylphosphonates, phosphonoacetates, thiophosphonoacetates and other variants of the phosphate backbone of native nucleic acids, such as those described herein. In some embodiments, a natural nucleotide comprises a naturally occurring base, sugar and internucleotidic linkage. As used herein, the term "nucleotide" also encompasses structural analogs used in lieu of natural or naturally-occurring nucleotides, such as modified nucleotides and nucleotide analogs. In some embodiments, a "nucleotide" refers to a nucleotide unit in an oligonucleotide or a nucleic acid.

[00099] Oligonucleotide: The term "oligonucleotide" refers to a polymer or oligomer of nucleotides, and may contain any combination of natural and non-natural nucleobases, sugars, and internucleotidic linkages.

[00100] Oligonucleotides can be single-stranded or double-stranded. A single-stranded oligonucleotide can have double-stranded regions (formed by two portions of the single-stranded oligonucleotide) and a double-stranded oligonucleotide, which comprises two oligonucleotide chains, can have single-stranded regions for example, at regions where the two oligonucleotide chains are not complementary to each other. Example oligonucleotides include, but are not limited to structural genes, genes including control and termination regions, self-replicating systems such as viral or plasmid DNA, single-stranded and double-stranded RNAi agents and other RNA interference reagents (RNAi agents or iRNA agents), shRNA, antisense oligonucleotides, ribozymes, microRNAs, microRNA mimics, supermirs, aptamers, antimirs, antagomirs, Ul adaptors, triplex-forming oligonucleotides, G-quadruplex oligonucleotides, RNA activators, immuno-stimulatory oligonucleotides, and decoy oligonucleotides.

[00101] Oligonucleotides of the present disclosure can be of various lengths. In particular embodiments, oligonucleotides can range from about 2 to about 200 nucleosides in length. In various related embodiments, oligonucleotides, single-stranded, double-stranded, or triple-stranded, can range in length from about 4 to about 10 nucleosides, from about 10 to about 50 nucleosides, from about 20 to about 50 nucleosides, from about 15 to about 30 nucleosides, from about 20 to about 30 nucleosides in length. In some embodiments, an oligonucleotide is from about 9 to about 39 nucleosides in length. In some embodiments, an oligonucleotide is from about 25 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 26 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 27 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 28 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 29 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 30 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 31 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 32 to about 70 nucleosides in length. In some embodiments, an oligonucleotide is from about 25 to about 60 nucleosides in length. In some embodiments, an oligonucleotide is from about 25 to about 50 nucleosides in length. In some embodiments, an oligonucleotide is from about 25 to about 40 nucleosides in length. In some embodiments, an oligonucleotide is from about 30 to about 40 nucleosides in length. In some embodiments, the oligonucleotide is at least 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 nucleosides in length. In some embodiments, an oligonucleotide is at least 4 nucleosides in length. In some embodiments, an oligonucleotide is at least 5 nucleosides in length. In some embodiments, an oligonucleotide is at least 6 nucleosides in length. In some embodiments, an oligonucleotide is at least 7 nucleosides in length. In some embodiments, an oligonucleotide is at least 8 nucleosides in length. In some embodiments, an oligonucleotide is at least 9 nucleosides in length. In some embodiments, an oligonucleotide is at least 10 nucleosides in length. In some embodiments, an oligonucleotide is at least 11 nucleosides in length. In some embodiments, an oligonucleotide is at least 12 nucleosides in length. In some embodiments, an oligonucleotide is at least 15 nucleosides in length. In some embodiments, an oligonucleotide is at least 15 nucleosides in length. In some embodiments, an oligonucleotide is at least 16 nucleosides in length. In some embodiments, an oligonucleotide is at least 17 nucleosides in length. In some embodiments, an oligonucleotide is at least 18 nucleosides in length. In some embodiments, an oligonucleotide is at least 19 nucleosides in length. In some embodiments, an oligonucleotide is at least 20 nucleosides in length. In some embodiments, an oligonucleotide is at least 25 nucleosides in length. In some embodiments, an oligonucleotide is at least 26 nucleosides in length. In some embodiments, an oligonucleotide is at least 27 nucleosides in length. In some embodiments, an oligonucleotide is at least 28 nucleosides in length. In some embodiments, an oligonucleotide is at least 29 nucleosides in length. In some embodiments, an oligonucleotide is at least 30 nucleosides in length. In some embodiments, an oligonucleotide is at least 31 nucleosides in length. In some embodiments, an oligonucleotide is at least 32 nucleosides in length. In some embodiments, an oligonucleotide is at least 33 nucleosides in length. In some embodiments, an oligonucleotide is at least 34 nucleosides in

length. In some embodiments, an oligonucleotide is at least 35 nucleosides in length. In some embodiments, an oligonucleotide is at least 36 nucleosides in length. In some embodiments, an oligonucleotide is at least 37 nucleosides in length. In some embodiments, an oligonucleotide is at least 38 nucleosides in length. In some embodiments, an oligonucleotide is at least 39 nucleosides in length. In some embodiments, an oligonucleotide is at least 40 nucleosides in length. In some embodiments, an oligonucleotide is 25 nucleosides in length. In some embodiments, an oligonucleotide is 26 nucleosides in length. In some embodiments, an oligonucleotide is 27 nucleosides in length. In some embodiments, an oligonucleotide is 28 nucleosides in length. In some embodiments, an oligonucleotide is 29 nucleosides in length. In some embodiments, an oligonucleotide is 30 nucleosides in length. In some embodiments, an oligonucleotide is 31 nucleosides in length. In some embodiments, an oligonucleotide is 32 nucleosides in length. In some embodiments, an oligonucleotide is 33 nucleosides in length. In some embodiments, an oligonucleotide is 34 nucleosides in length. In some embodiments, an oligonucleotide is 35 nucleosides in length. In some embodiments, an oligonucleotide is 36 nucleosides in length. In some embodiments, an oligonucleotide is 37 nucleosides in length. In some embodiments, an oligonucleotide is 38 nucleosides in length. In some embodiments, an oligonucleotide is 39 nucleosides in length. In some embodiments, an oligonucleotide is 40 nucleosides in length. In some embodiments, each nucleoside counted in an oligonucleotide length independently comprises a nucleobase comprising a ring having at least one nitrogen ring atom. In some embodiments, each nucleoside counted in an oligonucleotide length independently comprises A, T, C, G, or U, or optionally substituted A, T, C, G, or U, or an optionally substituted tautomer of A, T, C, G or U.

[00102] Oligonucleotide type: As used herein, the phrase "oligonucleotide type" is used to define an oligonucleotide that has a particular base sequence, pattern of backbone linkages (i.e., pattern of internucleotidic linkage types, for example, phosphate, phosphorothioate, phosphorothioate triester, etc.), pattern of backbone chiral centers [i.e., pattern of linkage phosphorus stereochemistry (Rp/Sp)], and pattern of backbone phosphorus modifications. In some embodiments, oligonucleotides of a common designated "type" are structurally identical to one another.

[00103] One of skill in the art will appreciate that synthetic methods of the present disclosure provide for a degree of control during the synthesis of an oligonucleotide strand such that each nucleotide unit of the oligonucleotide strand can be designed and/or selected in advance to have a particular stereochemistry at the linkage phosphorus and/or a particular modification at the linkage phosphorus, and/or a particular base, and/or a particular sugar. In some embodiments, an oligonucleotide strand is designed and/or selected in advance to have a particular combination of stereocenters at the linkage phosphorus. In some embodiments, an oligonucleotide strand is designed and/or determined to have a particular combination of modifications at the linkage phosphorus. In some embodiments, an oligonucleotide strand is designed and/or selected to have a particular combination of bases. In some embodiments, an oligonucleotide strand is designed and/or selected to have a particular combination of one or more of the above structural characteristics. In some embodiments, the present disclosure provides compositions comprising or consisting of a plurality of oligonucleotide

molecules (e.g., chirally controlled oligonucleotide compositions). In some embodiments, all such molecules are of the same type (i.e., are structurally identical to one another). In some embodiments, however, provided compositions comprise a plurality of oligonucleotides of different types, typically in pre-determined relative amounts.

[00104] Optionally Substituted: As described herein, compounds of the disclosure may contain optionally substituted, substituted and/or unsubstituted moieties. In general, the term "substituted," means that one or more hydrogens of the designated moiety are independently replaced with a substituent. Unless otherwise indicated, an "optionally substituted" group may independently have a substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with two or more substituents, the substituents may be either the same or different at every position. In some embodiments, an optionally substituted group is unsubstituted. In some embodiments, an optionally substituted group is substituted. Various substituents are described below.

[00105] Monovalent substituents are independently halogen; $-(CH_2)_{0-4}R^\circ$; $-(CH_2)_{0-4}OR^\circ$; $-O(CH_2)_{0-4}R^\circ$, $-O-(CH_2)_{0-4}C(O)OR^\circ$; $-(CH_2)_{0-4}CH(OR^\circ)_2$; $-(CH_2)_{0-4}Ph$, which may be substituted with R°; $-(CH_2)_{0-4}O(CH_2)_{0-1}Ph$ which may be substituted with R°; –CH=CHPh, which may be substituted with R°; $-(CH_2)_{0-4}O(CH_2)_{0-1}$-pyridyl which may be substituted with R°; $–NO_2$; –CN; $–N_3$; $-(CH_2)_{0-4}N(R^\circ)_2$; $-(CH_2)_{0-4}N(R^\circ)C(O)R^\circ$; $–N(R^\circ)C(S)R^\circ$; $-(CH_2)_{0-4}N(R^\circ)C(O)N(R^\circ)_2$; $–N(R^\circ)C(S)N(R^\circ)_2$; $-(CH_2)_{0-4}N(R^\circ)C(O)OR^\circ$; $–N(R^\circ)N(R^\circ)C(O)R^\circ$; $–N(R^\circ)N(R^\circ)C(O)N(R^\circ)_2$; $–N(R^\circ)N(R^\circ)C(O)OR^\circ$; $-(CH_2)_{0-4}C(O)R^\circ$; $–C(S)R^\circ$; $-(CH_2)_{0-4}C(O)OR^\circ$; $-(CH_2)_{0-4}C(O)SR^\circ$; $–(CH_2)_{0-4}C(O)OSi(R^\circ)_3$; $-(CH_2)_{0-4}OC(O)R^\circ$; $–OC(O)(CH_2)_{0-4}SR^\circ$, $–SC(S)SR^\circ$; $–(CH_2)_{0-4}SC(O)R^\circ$; $-(CH_2)_{0-4}C(O)N(R^\circ)_2$; $–C(S)N(R^\circ)_2$; $–C(S)SR^\circ$; $–SC(S)SR^\circ$, $-(CH_2)_{0-4}OC(O)N(R^\circ)_2$; $-C(O)N(OR^\circ)R^\circ$; $–C(O)C(O)R^\circ$; $–C(O)CH_2C(O)R^\circ$; $–C(NOR^\circ)R^\circ$; $-(CH_2)_{0-4}SSR^\circ$; $–(CH_2)_{0-4}S(O)_2R^\circ$; $–(CH_2)_{0-4}S(O)_2OR^\circ$; $-(CH_2)_{0-4}OS(O)_2R^\circ$; $–S(O)_2N(R^\circ)_2$; $-(CH_2)_{0-4}S(O)R^\circ$; $–N(R^\circ)S(O)_2N(R^\circ)_2$; $–N(R^\circ)S(O)_2R^\circ$; $–N(OR^\circ)R^\circ$; $–C(NH)N(R^\circ)_2$; $–Si(R^\circ)_3$; $–OSi(R^\circ)_3$; $–P(R^\circ)_2$; $–P(OR^\circ)_2$; $–OP(R^\circ)_2$; $–OP(OR^\circ)_2$; $–N(R^\circ)P(R^\circ)_2$; $–B(R^\circ)_2$; $–OB(R^\circ)_2$; $–P(O)(R^\circ)_2$; $–OP(O)(R^\circ)_2$; $–N(R^\circ)P(O)(R^\circ)_2$; –($C_{1-4}$ straight or branched alkylene)O–$N(R^\circ)_2$; or –(C_{1-4} straight or branched alkylene)C(O)O–$N(R^\circ)_2$; wherein each R° may be independently substituted as defined below and is independently hydrogen, C_{1-10} (e.g., C_{1-6}, C_{1-4}, etc.) aliphatic, C_{1-10} (e.g., C_{1-6}, C_{1-4}, etc.) heteroaliphatic having 1-5 heteroatoms independently selected from nitrogen, oxygen, sulfur, silicon and phosphorus, C_{6-10} (e.g., C_6, C_{10}, etc.) aryl, 5-10 (e.g., 5-9, 5-6, 5, 6, 9, 10, etc.) membered heteroaryl having 1-4 heteroatoms independently selected from nitrogen, oxygen and sulfur, $–CH_2–$(C_{6-10} (e.g., C_6, C_{10}, etc.) aryl), $–O(CH_2)_{0-1}$(C_{6-10} (e.g., C_6, C_{10}, etc.) aryl), $–CH_2–$(5-10 (e.g., 5-9, 5-6, 5, 6, 9, 10, etc.) membered heteroaryl having 1-4 heteroatoms independently selected from nitrogen, oxygen and sulfur), $–O(CH_2)_{0-1}$(5-10 (e.g., 5-9, 5-6, 5, 6, 9, 10, etc.) membered heteroaryl having 1-4 heteroatoms independently selected from nitrogen, oxygen and sulfur), a 3-10 (e.g., 3-6, 5-6, 3, 4, 5, 6, 7, 8, 9, 10, etc.) membered, monocyclic, bicyclic, or polycyclic, saturated, or partially unsaturated ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, sulfur, silicon and phosphorus, or, notwithstanding the

definition above, two independent occurrences of R°, taken together with their intervening atom(s), form a 3-10 (e.g., 3-6, 5-6, 3, 4, 5, 6, 7, 8, 9, 10, etc.) membered, monocyclic, bicyclic, or polycyclic, saturated, partially unsaturated or aromatic ring (for aromatic ring, 5-10 (e.g., 5-9, 5-6, 5, 6, 9, 10, etc.) membered) having, in addition to the intervening atom(s), 0-5 heteroatoms independently selected from nitrogen, oxygen, sulfur, silicon and phosphorus, which may be substituted as defined below.

[00106] Monovalent substituents on R° (or the ring formed by taking two independent occurrences of R° together with their intervening atoms), are independently halogen, $-(CH_2)_{0-2}R^{\bullet}$, $-(haloR^{\bullet})$, $-(CH_2)_{0-2}OH$, $-(CH_2)_{0-2}OR^{\bullet}$, $-(CH_2)_{0-2}CH(OR^{\bullet})_2$, $-O(haloR^{\bullet})$, $-CN$, $-N_3$, $-(CH_2)_{0-2}C(O)R^{\bullet}$, $-(CH_2)_{0-2}C(O)OH$, $-(CH_2)_{0-2}C(O)OR^{\bullet}$, $-(CH_2)_{0-2}SR^{\bullet}$, $-(CH_2)_{0-2}SH$, $-(CH_2)_{0-2}NH_2$, $-(CH_2)_{0-2}NHR^{\bullet}$, $-(CH_2)_{0-2}NR^{\bullet}_2$, $-NO_2$, $-SiR^{\bullet}_3$, $-OSiR^{\bullet}_3$, -C(O)SR$^{\bullet}$, $-(C_{1-4}$ straight or branched alkylene)C(O)OR$^{\bullet}$, or $-SSR^{\bullet}$ wherein each R$^{\bullet}$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently selected from C_{1-4} aliphatic, $-CH_2Ph$, $-O(CH_2)_{0-1}Ph$, or a 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur. Divalent substituents on a saturated carbon atom of R° are independently =O or =S.

[00107] Divalent substituents are independently the following: =O, =S, $=NNR^*_2$, =NNHC(O)R*, =NNHC(O)OR*, $=NNHS(O)_2R^*$, =NR*, =NOR*, $-O(C(R^*_2))_{2-3}O-$, or $-S(C(R^*_2))_{2-3}S-$, wherein each independent occurrence of R* is selected from hydrogen, C_{1-6} aliphatic which may be substituted as defined below, or an unsubstituted 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur. Divalent substituents that are bound to vicinal substitutable carbons of an "optionally substituted" group are independently $-O(CR^*_2)_{2-3}O-$, wherein each independent occurrence of R* is selected from hydrogen, C_{1-6} aliphatic which may be substituted as defined below, or an unsubstituted 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[00108] Substituents on the aliphatic group of R* are independently halogen, $-R^{\bullet}$, -(haloR$^{\bullet}$), -OH, $-OR^{\bullet}$, $-O(haloR^{\bullet})$, -CN, -C(O)OH, $-C(O)OR^{\bullet}$, $-NH_2$, $-NHR^{\bullet}$, $-NR^{\bullet}_2$, or $-NO_2$, wherein each R$^{\bullet}$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently C_{1-4} aliphatic, $-CH_2Ph$, $-O(CH_2)_{0-1}Ph$, or a 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[00109] Substituents on a substitutable nitrogen are independently $-R^{\dagger}$, $-NR^{\dagger}_2$, $-C(O)R^{\dagger}$, $-C(O)OR^{\dagger}$, $-C(O)C(O)R^{\dagger}$, $-C(O)CH_2C(O)R^{\dagger}$, $-S(O)_2R^{\dagger}$, $-S(O)_2NR^{\dagger}_2$, $-C(S)NR^{\dagger}_2$, $-C(NH)NR^{\dagger}_2$, or $-N(R^{\dagger})S(O)_2R^{\dagger}$; wherein each R† is independently hydrogen, C_{1-6} aliphatic which may be substituted as defined below, unsubstituted $-OPh$, or an unsubstituted 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or

aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or, notwithstanding the definition above, two independent occurrences of $R^{\dagger}$, taken together with their intervening atom(s) form an unsubstituted 3–12 (e.g., 3-10, 3-6, 5-10, 5-6, 3, 4, 5, 6, 7, 8, 9, 10, etc.) membered saturated, partially unsaturated, or aryl mono– or bicyclic ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[00110] Substituents on the aliphatic group of $R^{\dagger}$ are independently halogen, –$R^{\bullet}$, -(halo$R^{\bullet}$), –OH, –$OR^{\bullet}$, –O(halo$R^{\bullet}$), –CN, –C(O)OH, –C(O)$OR^{\bullet}$, –NH_2, –$NHR^{\bullet}$, –$NR^{\bullet}_2$, or –NO_2, wherein each $R^{\bullet}$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently C_{1-4} aliphatic, –CH_2Ph, –$O(CH_2)_{0-1}$Ph, or a 3-6 (e.g., 3-5, 5-6, etc.)-membered saturated, partially unsaturated, or aromatic ring (for aromatic ring, 5- or 6-membered) having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[00111] P-modification: as used herein, the term "P-modification" refers to any modification at the linkage phosphorus other than a stereochemical modification. In some embodiments, a P-modification comprises addition, substitution, or removal of a pendant moiety covalently attached to a linkage phosphorus.

[00112] Partially unsaturated: As used herein, the term "partially unsaturated" refers to a ring moiety that includes at least one double or triple bond. The term "partially unsaturated" is intended to encompass rings having multiple sites of unsaturation, but is not intended to include aryl or heteroaryl moieties, as herein defined.

[00113] Pharmaceutical composition: As used herein, the term "pharmaceutical composition" refers to an active agent, formulated together with one or more pharmaceutically acceptable carriers. In some embodiments, an active agent is present in unit dose amount appropriate for administration in a therapeutic regimen that shows a statistically significant probability of achieving a predetermined therapeutic effect when administered to a relevant population. In some embodiments, pharmaceutical compositions may be specially formulated for administration in solid or liquid form, including those adapted for the following: oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; parenteral administration, for example, by subcutaneous, intramuscular, intravenous or epidural injection as, for example, a sterile solution or suspension, or sustained-release formulation; topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin, lungs, or oral cavity; intravaginally or intrarectally, for example, as a pessary, cream, or foam; sublingually; ocularly; transdermally; or nasally, pulmonary, and to other mucosal surfaces.

[00114] Pharmaceutically acceptable: As used herein, the phrase "pharmaceutically acceptable" refers to those compounds, materials, compositions and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[00115] Pharmaceutically acceptable carrier: As used herein, the term "pharmaceutically acceptable carrier" means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, or solvent encapsulating material, involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: sugars, such as lactose, glucose and sucrose; starches, such as corn starch and potato starch; cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients, such as cocoa butter and suppository waxes; oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols, such as propylene glycol; polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; esters, such as ethyl oleate and ethyl laurate; agar; buffering agents, such as magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol; pH buffered solutions; polyesters, polycarbonates and/or polyanhydrides; and other non-toxic compatible substances employed in pharmaceutical formulations.

[00116] Pharmaceutically acceptable salt: The term "pharmaceutically acceptable salt", as used herein, refers to salts of such compounds that are appropriate for use in pharmaceutical contexts, i.e., salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like, and are commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge, et al. describes pharmaceutically acceptable salts in detail in J. Pharmaceutical Sciences, 66: 1-19 (1977). In some embodiments, pharmaceutically acceptable salt include, but are not limited to, nontoxic acid addition salts, which are salts of an amino group formed with inorganic acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid and perchloric acid or with organic acids such as acetic acid, maleic acid, tartaric acid, citric acid, succinic acid or malonic acid or by using other methods used in the art such as ion exchange. In some embodiments, pharmaceutically acceptable salts include, but are not limited to, adipate, alginate, ascorbate, aspartate, benzenesulfonate, benzoate, bisulfate, borate, butyrate, camphorate, camphorsulfonate, citrate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, formate, fumarate, glucoheptonate, glycerophosphate, gluconate, hemisulfate, heptanoate, hexanoate, hydroiodide, 2-hydroxy-ethanesulfonate, lactobionate, lactate, laurate, lauryl sulfate, malate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oleate, oxalate, palmitate, pamoate, pectinate, persulfate, 3-phenylpropionate, phosphate, picrate, pivalate, propionate, stearate, succinate, sulfate, tartrate, thiocyanate, p-toluenesulfonate, undecanoate, valerate salts, and the like. In some embodiments, a provided compound comprises one or more acidic groups, e.g., an oligonucleotide, and a pharmaceutically acceptable salt is an alkali, alkaline earth metal, or ammonium (e.g., an ammonium salt of $N(R)_3$, wherein each R is independently defined and described in the present disclosure) salt. Representative alkali or alkaline earth metal salts include sodium, lithium, potassium, calcium, magnesium, and the like. In some embodiments, a

pharmaceutically acceptable salt is a sodium salt. In some embodiments, a pharmaceutically acceptable salt is a potassium salt. In some embodiments, a pharmaceutically acceptable salt is a calcium salt. In some embodiments, pharmaceutically acceptable salts include, when appropriate, nontoxic ammonium, quaternary ammonium, and amine cations formed using counterions such as halide, hydroxide, carboxylate, sulfate, phosphate, nitrate, alkyl having from 1 to 6 carbon atoms, sulfonate and aryl sulfonate. In some embodiments, a provided compound comprises more than one acid groups, for example, an oligonucleotide may comprise two or more acidic groups (e.g., in natural phosphate linkages and/or modified internucleotidic linkages). In some embodiments, a pharmaceutically acceptable salt, or generally a salt, of such a compound comprises two or more cations, which can be the same or different. In some embodiments, in a pharmaceutically acceptable salt (or generally, a salt), all ionizable hydrogen (e.g., in an aqueous solution with a pKa no more than about 11, 10, 9, 8, 7, 6, 5, 4, 3, or 2; in some embodiments, no more than about 7; in some embodiments, no more than about 6; in some embodiments, no more than about 5; in some embodiments, no more than about 4; in some embodiments, no more than about 3) in the acidic groups are replaced with cations. In some embodiments, each phosphorothioate and phosphate group independently exists in its salt form (e.g., if sodium salt, –O–P(O)(SNa)–O– and –O–P(O)(ONa)–O–, respectively). In some embodiments, each phosphorothioate and phosphate internucleotidic linkage independently exists in its salt form (e.g., if sodium salt, –O–P(O)(SNa)–O– and –O–P(O)(ONa)–O–, respectively). In some embodiments, a pharmaceutically acceptable salt is a sodium salt of an oligonucleotide. In some embodiments, a pharmaceutically acceptable salt is a sodium salt of an oligonucleotide, wherein each acidic phosphate and modified phosphate group (e.g., phosphorothioate, phosphate, etc.), if any, exists as a salt form (all sodium salt).

[00117] Predetermined: By predetermined (or pre-determined) is meant deliberately selected or non-random or controlled, for example as opposed to randomly occurring, random, or achieved without control. Those of ordinary skill in the art, reading the present specification, will appreciate that the present disclosure provides technologies that permit selection of particular chemistry and/or stereochemistry features to be incorporated into oligonucleotide compositions, and further permits controlled preparation of oligonucleotide compositions having such chemistry and/or stereochemistry features. Such provided compositions are "predetermined" as described herein. Compositions that may contain certain oligonucleotides because they happen to have been generated through a process that are not controlled to intentionally generate the particular chemistry and/or stereochemistry features are not "predetermined" compositions. In some embodiments, a predetermined composition is one that can be intentionally reproduced (e.g., through repetition of a controlled process). In some embodiments, a predetermined level of a plurality of oligonucleotides in a composition means that the absolute amount, and/or the relative amount (ratio, percentage, etc.) of the plurality of oligonucleotides in the composition is controlled. In some embodiments, a predetermined level of a plurality of oligonucleotides in a composition is achieved through chirally controlled oligonucleotide preparation.

[00118] Protecting group: The term "protecting group," as used herein, is well known in the art and includes those described in detail in Protecting Groups in Organic Synthesis, T. W. Greene and P. G. M. Wuts,

3rd edition, John Wiley & Sons, 1999, the entirety of which is incorporated herein by reference. Also included are those protecting groups specially adapted for nucleoside and nucleotide chemistry described in Current Protocols in Nucleic Acid Chemistry, edited by Serge L. Beaucage et al. 06/2012, the entirety of Chapter 2 is incorporated herein by reference. Suitable amino–protecting groups include methyl carbamate, ethyl carbamante, 9–fluorenylmethyl carbamate (Fmoc), 9–(2–sulfo)fluorenylmethyl carbamate, 9–(2,7–dibromo)fluoroenylmethyl carbamate, 2,7–di–t–butyl–[9–(10,10–dioxo–10,10,10,10–tetrahydrothioxanthyl)]methyl carbamate (DBD–Tmoc), 4–methoxyphenacyl carbamate (Phenoc), 2,2,2–trichloroethyl carbamate (Troc), 2–trimethylsilylethyl carbamate (Teoc), 2–phenylethyl carbamate (hZ), 1–(1–adamantyl)–1–methylethyl carbamate (Adpoc), 1,1–dimethyl–2–haloethyl carbamate, 1,1–dimethyl–2,2–dibromoethyl carbamate (DB–t–BOC), 1,1–dimethyl–2,2,2–trichloroethyl carbamate (TCBOC), 1–methyl–1–(4–biphenylyl)ethyl carbamate (Bpoc), 1–(3,5–di–t–butylphenyl)–1–methylethyl carbamate (t–Bumeoc), 2–(2'– and 4'–pyridyl)ethyl carbamate (Pyoc), 2–(N,N–dicyclohexylcarboxamido)ethyl carbamate, t–butyl carbamate (BOC), 1–adamantyl carbamate (Adoc), vinyl carbamate (Voc), allyl carbamate (Alloc), 1–isopropylallyl carbamate (Ipaoc), cinnamyl carbamate (Coc), 4–nitrocinnamyl carbamate (Noc), 8–quinolyl carbamate, N–hydroxypiperidinyl carbamate, alkyldithio carbamate, benzyl carbamate (Cbz), p–methoxybenzyl carbamate (Moz), p–nitobenzyl carbamate, p–bromobenzyl carbamate, p–chlorobenzyl carbamate, 2,4–dichlorobenzyl carbamate, 4–methylsulfinylbenzyl carbamate (Msz), 9–anthrylmethyl carbamate, diphenylmethyl carbamate, 2–methylthioethyl carbamate, 2–methylsulfonylethyl carbamate, 2–(p–toluenesulfonyl)ethyl carbamate, [2–(1,3–dithianyl)]methyl carbamate (Dmoc), 4–methylthiophenyl carbamate (Mtpc), 2,4–dimethylthiophenyl carbamate (Bmpc), 2–phosphonioethyl carbamate (Peoc), 2–triphenylphosphonioisopropyl carbamate (Ppoc), 1,1–dimethyl–2–cyanoethyl carbamate, m–chloro–p–acyloxybenzyl carbamate, p–(dihydroxyboryl)benzyl carbamate, 5–benzisoxazolylmethyl carbamate, 2–(trifluoromethyl)–6–chromonylmethyl carbamate (Tcroc), m–nitrophenyl carbamate, 3,5–dimethoxybenzyl carbamate, o–nitrobenzyl carbamate, 3,4–dimethoxy–6–nitrobenzyl carbamate, phenyl(o–nitrophenyl)methyl carbamate, phenothiazinyl–(10)–carbonyl derivative, N'–p–toluenesulfonylaminocarbonyl derivative, N'–phenylaminothiocarbonyl derivative, t–amyl carbamate, S–benzyl thiocarbamate, p–cyanobenzyl carbamate, cyclobutyl carbamate, cyclohexyl carbamate, cyclopentyl carbamate, cyclopropylmethyl carbamate, p–decyloxybenzyl carbamate, 2,2–dimethoxycarbonylvinyl carbamate, o–(N,N–dimethylcarboxamido)benzyl carbamate, 1,1–dimethyl–3–(N,N–dimethylcarboxamido)propyl carbamate, 1,1–dimethylpropynyl carbamate, di(2–pyridyl)methyl carbamate, 2–furanylmethyl carbamate, 2–iodoethyl carbamate, isobornyl carbamate, isobutyl carbamate, isonicotinyl carbamate, p–(p'–methoxyphenylazo)benzyl carbamate, 1–methylcyclobutyl carbamate, 1–methylcyclohexyl carbamate, 1–methyl–1–cyclopropylmethyl carbamate, 1–methyl–1–(3,5–dimethoxyphenyl)ethyl carbamate, 1–methyl–1–(p–phenylazophenyl)ethyl carbamate, 1–methyl–1–phenylethyl carbamate, 1–methyl–1–(4–pyridyl)ethyl carbamate, phenyl carbamate, p–(phenylazo)benzyl carbamate, 2,4,6–tri–t–butylphenyl carbamate, 4–(trimethylammonium)benzyl carbamate, 2,4,6–trimethylbenzyl carbamate, formamide, acetamide, chloroacetamide, trichloroacetamide, trifluoroacetamide,

phenylacetamide, 3–phenylpropanamide, picolinamide, 3–pyridylcarboxamide, N–benzoylphenylalanyl derivative, benzamide, p–phenylbenzamide, o–nitophenylacetamide, o–nitrophenoxyacetamide, acetoacetamide, (N'–dithiobenzyloxycarbonylamino)acetamide, 3–(p–hydroxyphenyl)propanamide, 3–(o–nitrophenyl)propanamide, 2–methyl–2–(o–nitrophenoxy)propanamide, 2–methyl–2–(o–phenylazophenoxy)propanamide, 4–chlorobutanamide, 3–methyl–3–nitrobutanamide, o–nitrocinnamide, N–acetylmethionine derivative, o–nitrobenzamide, o–(benzoyloxymethyl)benzamide, 4,5–diphenyl–3–oxazolin–2–one, N–phthalimide, N–dithiasuccinimide (Dts), N–2,3–diphenylmaleimide, N–2,5–dimethylpyrrole, N–1,1,4,4–tetramethyldisilylazacyclopentane adduct (STABASE), 5–substituted 1,3–dimethyl–1,3,5–triazacyclohexan–2–one, 5–substituted 1,3–dibenzyl–1,3,5–triazacyclohexan–2–one, 1–substituted 3,5–dinitro–4–pyridone, N–methylamine, N–allylamine, N–[2–(trimethylsilyl)ethoxy]methylamine (SEM), N–3–acetoxypropylamine, N–(1–isopropyl–4–nitro–2–oxo–3–pyroolin–3–yl)amine, quaternary ammonium salts, N–benzylamine, N–di(4–methoxyphenyl)methylamine, N–5–dibenzosuberylamine, N–triphenylmethylamine (Tr), N–[(4–methoxyphenyl)diphenylmethyl]amine (MMTr), N–9–phenylfluorenylamine (PhF), N–2,7–dichloro–9–fluorenylmethyleneamine, N–ferrocenylmethylamino (Fcm), N–2–picolylamino N'–oxide, N–1,1–dimethylthiomethyleneamine, N–benzylideneamine, N–p–methoxybenzylideneamine, N–diphenylmethyleneamine, N–[(2–pyridyl)mesityl]methyleneamine, N–(N',N'–dimethylaminomethylene)amine, N,N'–isopropylidenediamine, N–p–nitrobenzylideneamine, N–salicylideneamine, N–5–chlorosalicylideneamine, N–(5–chloro–2–hydroxyphenyl)phenylmethyleneamine, N–cyclohexylideneamine, N–(5,5–dimethyl–3–oxo–1–cyclohexenyl)amine, N–borane derivative, N–diphenylborinic acid derivative, N–[phenyl(pentacarbonylchromium– or tungsten)carbonyl]amine, N–copper chelate, N–zinc chelate, N–nitroamine, N–nitrosoamine, amine N–oxide, diphenylphosphinamide (Dpp), dimethylthiophosphinamide (Mpt), diphenylthiophosphinamide (Ppt), dialkyl phosphoramidates, dibenzyl phosphoramidate, diphenyl phosphoramidate, benzenesulfenamide, o–nitrobenzenesulfenamide (Nps), 2,4–dinitrobenzenesulfenamide, pentachlorobenzenesulfenamide, 2–nitro–4–methoxybenzenesulfenamide, triphenylmethylsulfenamide, 3–nitropyridinesulfenamide (Npys), p–toluenesulfonamide (Ts), benzenesulfonamide, 2,3,6,–trimethyl–4–methoxybenzenesulfonamide (Mtr), 2,4,6–trimethoxybenzenesulfonamide (Mtb), 2,6–dimethyl–4–methoxybenzenesulfonamide (Pme), 2,3,5,6–tetramethyl–4–methoxybenzenesulfonamide (Mte), 4–methoxybenzenesulfonamide (Mbs), 2,4,6–trimethylbenzenesulfonamide (Mts), 2,6–dimethoxy–4–methylbenzenesulfonamide (iMds), 2,2,5,7,8–pentamethylchroman–6–sulfonamide (Pmc), methanesulfonamide (Ms), β–trimethylsilylethanesulfonamide (SES), 9–anthracenesulfonamide, 4–(4',8'–dimethoxynaphthylmethyl)benzenesulfonamide (DNMBS), benzylsulfonamide, trifluoromethylsulfonamide, and phenacylsulfonamide.

[00119] Suitably protected carboxylic acids further include, but are not limited to, silyl–, alkyl–, alkenyl–, aryl–, and arylalkyl–protected carboxylic acids. Examples of suitable silyl groups include trimethylsilyl, triethylsilyl, t–butyldimethylsilyl, t–butyldiphenylsilyl, triisopropylsilyl, and the like. Examples of suitable alkyl groups include methyl, benzyl, p–methoxybenzyl, 3,4–dimethoxybenzyl, trityl, t–butyl, tetrahydropyran–

2–yl. Examples of suitable alkenyl groups include allyl. Examples of suitable aryl groups include optionally substituted phenyl, biphenyl, or naphthyl. Examples of suitable arylalkyl groups include optionally substituted benzyl (e.g., p–methoxybenzyl (MPM), 3,4–dimethoxybenzyl, O–nitrobenzyl, p–nitrobenzyl, p–halobenzyl, 2,6–dichlorobenzyl, p–cyanobenzyl), and 2– and 4–picolyl.

[00120] Suitable hydroxyl protecting groups include methyl, methoxylmethyl (MOM), methylthiomethyl (MTM), t–butylthiomethyl, (phenyldimethylsilyl)methoxymethyl (SMOM), benzyloxymethyl (BOM), p–methoxybenzyloxymethyl (PMBM), (4–methoxyphenoxy)methyl (p–AOM), guaiacolmethyl (GUM), t–butoxymethyl, 4–pentenyloxymethyl (POM), siloxymethyl, 2–methoxyethoxymethyl (MEM), 2,2,2–trichloroethoxymethyl, bis(2–chloroethoxy)methyl, 2–(trimethylsilyl)ethoxymethyl (SEMOR), tetrahydropyranyl (THP), 3–bromotetrahydropyranyl, tetrahydrothiopyranyl, 1–methoxycyclohexyl, 4–methoxytetrahydropyranyl (MTHP), 4–methoxytetrahydrothiopyranyl, 4–methoxytetrahydrothiopyranyl S,S–dioxide, 1–[(2–chloro–4–methyl)phenyl]–4–methoxypiperidin–4–yl (CTMP), 1,4–dioxan–2–yl, tetrahydrofuranyl, tetrahydrothiofuranyl, 2,3,3a,4,5,6,7,7a–octahydro–7,8,8–trimethyl–4,7–methanobenzofuran–2–yl, 1–ethoxyethyl, 1–(2–chloroethoxy)ethyl, 1–methyl–1–methoxyethyl, 1–methyl–1–benzyloxyethyl, 1–methyl–1–benzyloxy–2–fluoroethyl, 2,2,2–trichloroethyl, 2–trimethylsilylethyl, 2–(phenylselenyl)ethyl, t–butyl, allyl, p–chlorophenyl, p–methoxyphenyl, 2,4–dinitrophenyl, benzyl, p–methoxybenzyl, 3,4–dimethoxybenzyl, o–nitrobenzyl, p–nitrobenzyl, p–halobenzyl, 2,6–dichlorobenzyl, p–cyanobenzyl, p–phenylbenzyl, 2–picolyl, 4–picolyl, 3–methyl–2–picolyl N–oxido, diphenylmethyl, p,p'–dinitrobenzhydryl, 5–dibenzosuberyl, triphenylmethyl, α–naphthyldiphenylmethyl, p–methoxyphenyldiphenylmethyl, di(p–methoxyphenyl)phenylmethyl, tri(p–methoxyphenyl)methyl, 4–(4''–bromophenacyloxyphenyl)diphenylmethyl, 4,4',4''–tris(4,5–dichlorophthalimidophenyl)methyl, 4,4',4''–tris(levulinoyloxyphenyl)methyl, 4,4',4''–tris(benzoyloxyphenyl)methyl, 3–(imidazol–1–yl)bis(4',4''–dimethoxyphenyl)methyl, 1,1–bis(4–methoxyphenyl)–1'–pyrenylmethyl, 9–anthryl, 9–(9–phenyl)xanthenyl, 9–(9–phenyl–10–oxo)anthryl, 1,3–benzodithiolan–2–yl, benzisothiazolyl S,S–dioxido, trimethylsilyl (TMS), triethylsilyl (TES), triisopropylsilyl (TIPS), dimethylisopropylsilyl (IPDMS), diethylisopropylsilyl (DEIPS), dimethylthexylsilyl, t–butyldimethylsilyl (TBDMS), t–butyldiphenylsilyl (TBDPS), tribenzylsilyl, tri–p–xylylsilyl, triphenylsilyl, diphenylmethylsilyl (DPMS), t–butylmethoxyphenylsilyl (TBMPS), formate, benzoylformate, acetate, chloroacetate, dichloroacetate, trichloroacetate, trifluoroacetate, methoxyacetate, triphenylmethoxyacetate, phenoxyacetate, p–chlorophenoxyacetate, 3–phenylpropionate, 4–oxopentanoate (levulinate), 4,4–(ethylenedithio)pentanoate (levulinoyldithioacetal), pivaloate, adamantoate, crotonate, 4–methoxycrotonate, benzoate, p–phenylbenzoate, 2,4,6–trimethylbenzoate (mesitoate), alkyl methyl carbonate, 9–fluorenylmethyl carbonate (Fmoc), alkyl ethyl carbonate, alkyl 2,2,2–trichloroethyl carbonate (Troc), 2–(trimethylsilyl)ethyl carbonate (TMSEC), 2–(phenylsulfonyl) ethyl carbonate (Psec), 2–(triphenylphosphonio) ethyl carbonate (Peoc), alkyl isobutyl carbonate, alkyl vinyl carbonate alkyl allyl carbonate, alkyl p–nitrophenyl carbonate, alkyl benzyl carbonate, alkyl p–methoxybenzyl carbonate, alkyl 3,4–dimethoxybenzyl carbonate, alkyl o–nitrobenzyl carbonate, alkyl p–nitrobenzyl carbonate, alkyl S–benzyl thiocarbonate, 4–

ethoxy–1–napththyl carbonate, methyl dithiocarbonate, 2–iodobenzoate, 4–azidobutyrate, 4–nitro–4–methylpentanoate, o–(dibromomethyl)benzoate, 2–formylbenzenesulfonate, 2–(methylthiomethoxy)ethyl, 4–(methylthiomethoxy)butyrate, 2–(methylthiomethoxymethyl)benzoate, 2,6–dichloro–4–methylphenoxyacetate, 2,6–dichloro–4–(1,1,3,3–tetramethylbutyl)phenoxyacetate, 2,4–bis(1,1–dimethylpropyl)phenoxyacetate, chlorodiphenylacetate, isobutyrate, monosuccinoate, (E)–2–methyl–2–butenoate, o–(methoxycarbonyl)benzoate, α–naphthoate, nitrate, alkyl N,N,N',N'–tetramethylphosphorodiamidate, alkyl N–phenylcarbamate, borate, dimethylphosphinothioyl, alkyl 2,4–dinitrophenylsulfenate, sulfate, methanesulfonate (mesylate), benzylsulfonate, and tosylate (Ts). For protecting 1,2– or 1,3–diols, the protecting groups include methylene acetal, ethylidene acetal, 1–t–butylethylidene ketal, 1–phenylethylidene ketal, (4–methoxyphenyl)ethylidene acetal, 2,2,2–trichloroethylidene acetal, acetonide, cyclopentylidene ketal, cyclohexylidene ketal, cycloheptylidene ketal, benzylidene acetal, p–methoxybenzylidene acetal, 2,4–dimethoxybenzylidene ketal, 3,4–dimethoxybenzylidene acetal, 2–nitrobenzylidene acetal, methoxymethylene acetal, ethoxymethylene acetal, dimethoxymethylene ortho ester, 1–methoxyethylidene ortho ester, 1–ethoxyethylidine ortho ester, 1,2–dimethoxyethylidene ortho ester, α–methoxybenzylidene ortho ester, 1–(N,N–dimethylamino)ethylidene derivative, α–(N,N'–dimethylamino)benzylidene derivative, 2–oxacyclopentylidene ortho ester, di–t–butylsilylene group (DTBS), 1,3–(1,1,3,3–tetraisopropyldisiloxanylidene) derivative (TIPDS), tetra–t–butoxydisiloxane–1,3–diylidene derivative (TBDS), cyclic carbonates, cyclic boronates, ethyl boronate, and phenyl boronate.

[00121] In some embodiments, a hydroxyl protecting group is acetyl, t-butyl, tbutoxymethyl, methoxymethyl, tetrahydropyranyl, 1 -ethoxyethyl, 1 -(2-chloroethoxy)ethyl, 2- trimethylsilylethyl, p-chlorophenyl, 2,4-dinitrophenyl, benzyl, benzoyl, p-phenylbenzoyl, 2,6- dichlorobenzyl, diphenylmethyl, p-nitrobenzyl, triphenylmethyl (trityl), 4,4'-dimethoxytrityl, trimethylsilyl, triethylsilyl, t-butyldimethylsilyl, t-butyldiphenylsilyl, triphenylsilyl, triisopropylsilyl, benzoylformate, chloroacetyl, trichloroacetyl, trifluoroacetyl, pivaloyl, 9- fluorenylmethyl carbonate, mesylate, tosylate, triflate, trityl, monomethoxytrityl (MMTr), 4,4'-dimethoxytrityl, (DMTr) and 4,4',4"-trimethoxytrityl (TMTr), 2-cyanoethyl (CE or Cne), 2-(trimethylsilyl)ethyl (TSE), 2-(2-nitrophenyl)ethyl, 2-(4-cyanophenyl)ethyl 2-(4-nitrophenyl)ethyl (NPE), 2-(4-nitrophenylsulfonyl)ethyl, 3,5-dichlorophenyl, 2,4-dimethylphenyl, 2-nitrophenyl, 4-nitrophenyl, 2,4,6-trimethylphenyl, 2-(2-nitrophenyl)ethyl, butylthiocarbonyl, 4,4',4"-tris(benzoyloxy)trityl, diphenylcarbamoyl, levulinyl, 2-(dibromomethyl)benzoyl (Dbmb), 2-(isopropylthiomethoxymethyl)benzoyl (Ptmt), 9-phenylxanthen-9-yl (pixyl) or 9-(p-methoxyphenyl)xanthine-9-y l (MOX). In some embodiments, each of the hydroxyl protecting groups is, independently selected from acetyl, benzyl, t- butyldimethylsilyl, t-butyldiphenylsilyl and 4,4'-dimethoxytrityl. In some embodiments, the hydroxyl protecting group is selected from the group consisting of trityl, monomethoxytrityl and 4,4'-dimethoxytrityl group. In some embodiments, a phosphorous linkage protecting group is a group attached to the phosphorous linkage (e.g., an internucleotidic linkage) throughout oligonucleotide synthesis. In some embodiments, a protecting group is attached to a sulfur

atom of an phosphorothioate group. In some embodiments, a protecting group is attached to an oxygen atom of an internucleotide phosphorothioate linkage. In some embodiments, a protecting group is attached to an oxygen atom of the internucleotide phosphate linkage. In some embodiments a protecting group is 2-cyanoethyl (CE or Cne), 2-trimethylsilylethyl, 2-nitroethyl, 2-sulfonylethyl, methyl, benzyl, o-nitrobenzyl, 2-(p-nitrophenyl)ethyl (NPE or Npe), 2-phenylethyl, 3-(N-tert-butylcarboxamido)-1-propyl, 4-oxopentyl, 4-methylthio-1-butyl, 2-cyano-1,1-dimethylethyl, 4-N-methylaminobutyl, 3-(2-pyridyl)-1-propyl, 2-[N-methyl-N-(2-pyridyl)]aminoethyl, 2-(N-formyl,N-methyl)aminoethyl, or 4-[N-methyl-N-(2,2,2-trifluoroacetyl)amino]butyl.

[00122] Subject: As used herein, the term "subject" or "test subject" refers to any organism to which a compound (e.g., an oligonucleotide) or composition is administered in accordance with the present disclosure e.g., for experimental, diagnostic, prophylactic and/or therapeutic purposes. Typical subjects include animals (e.g., mammals such as mice, rats, rabbits, non-human primates, and humans; insects; worms; etc.) and plants. In some embodiments, a subject is a human. In some embodiments, a subject may be suffering from and/or susceptible to a disease, disorder and/or condition.

[00123] Substantially: As used herein, the term "substantially" refers to the qualitative condition of exhibiting total or near-total extent or degree of a characteristic or property of interest. A base sequence which is substantially identical or complementary to a second sequence is not fully identical or complementary to the second sequence, but is mostly or nearly identical or complementary to the second sequence. In some embodiments, an oligonucleotide with a substantially complementary sequence to another oligonucleotide or nucleic acid forms duplex with the oligonucleotide or nucleic acid in a similar fashion as an oligonucleotide with a fully complementary sequence. In addition, one of ordinary skill in the biological and/or chemical arts will understand that biological and chemical phenomena rarely, if ever, go to completion and/or proceed to completeness or achieve or avoid an absolute result. The term "substantially" is therefore used herein to capture the potential lack of completeness inherent in many biological and/or chemical phenomena.

[00124] Sugar: The term "sugar" refers to a monosaccharide or polysaccharide in closed and/or open form. In some embodiments, sugars are monosaccharides. In some embodiments, sugars are polysaccharides. Sugars include, but are not limited to, ribose, deoxyribose, pentofuranose, pentopyranose, and hexopyranose moieties. As used herein, the term "sugar" also encompasses structural analogs used in lieu of conventional sugar molecules, such as glycol, polymer of which forms the backbone of the nucleic acid analog, glycol nucleic acid ("GNA"), etc. As used herein, the term "sugar" also encompasses structural analogs used in lieu of natural or naturally-occurring nucleotides, such as modified sugars and nucleotide sugars. In some embodiments, a sugar is a RNA or DNA sugar (ribose or deoxyribose). In some embodiments, a sugar is a modified ribose or deoxyribose sugar, e.g., 2'-modified, 5'-modified, etc. As described herein, in some embodiments, when used in oligonucleotides and/or nucleic acids, modified sugars may provide one or more desired properties, activities, etc. In some embodiments, a sugar is optionally substituted ribose or deoxyribose. In some embodiments, a "sugar" refers to a sugar unit in an oligonucleotide or a nucleic acid.

[00125] Susceptible to: An individual who is "susceptible to" a disease, disorder and/or condition is one who has a higher risk of developing the disease, disorder and/or condition than does a member of the general public. In some embodiments, an individual who is susceptible to a disease, disorder and/or condition is predisposed to have that disease, disorder and/or condition. In some embodiments, an individual who is susceptible to a disease, disorder and/or condition may not have been diagnosed with the disease, disorder and/or condition. In some embodiments, an individual who is susceptible to a disease, disorder and/or condition may exhibit symptoms of the disease, disorder and/or condition. In some embodiments, an individual who is susceptible to a disease, disorder and/or condition may not exhibit symptoms of the disease, disorder and/or condition. In some embodiments, an individual who is susceptible to a disease, disorder, and/or condition will develop the disease, disorder, and/or condition. In some embodiments, an individual who is susceptible to a disease, disorder, and/or condition will not develop the disease, disorder, and/or condition.

[00126] Therapeutic agent: As used herein, the term "therapeutic agent" in general refers to any agent that elicits a desired effect (e.g., a desired biological, clinical, or pharmacological effect) when administered to a subject. In some embodiments, an agent is considered to be a therapeutic agent if it demonstrates a statistically significant effect across an appropriate population. In some embodiments, an appropriate population is a population of subjects suffering from and/or susceptible to a disease, disorder or condition. In some embodiments, an appropriate population is a population of model organisms. In some embodiments, an appropriate population may be defined by one or more criterion such as age group, gender, genetic background, preexisting clinical conditions, prior exposure to therapy. In some embodiments, a therapeutic agent is a substance that alleviates, ameliorates, relieves, inhibits, prevents, delays onset of, reduces severity of, and/or reduces incidence of one or more symptoms or features of a disease, disorder, and/or condition in a subject when administered to the subject in an effective amount. In some embodiments, a "therapeutic agent" is an agent that has been or is required to be approved by a government agency before it can be marketed for administration to humans. In some embodiments, a "therapeutic agent" is an agent for which a medical prescription is required for administration to humans. In some embodiments, a therapeutic agent is a provided compound, e.g., a provided oligonucleotide.

[00127] Therapeutically effective amount: As used herein, the term "therapeutically effective amount" means an amount of a substance (e.g., a therapeutic agent, composition, and/or formulation) that elicits a desired biological response when administered as part of a therapeutic regimen. In some embodiments, a therapeutically effective amount of a substance is an amount that is sufficient, when administered to a subject suffering from or susceptible to a disease, disorder, and/or condition, to treat, diagnose, prevent, and/or delay the onset of the disease, disorder, and/or condition. As will be appreciated by those of ordinary skill in this art, the effective amount of a substance may vary depending on such factors as the desired biological endpoint, the substance to be delivered, the target cell or tissue, etc. For example, the effective amount of compound in a formulation to treat a disease, disorder, and/or condition is the amount that alleviates, ameliorates, relieves, inhibits, prevents, delays onset of, reduces severity of and/or reduces incidence of one or more symptoms or

features of the disease, disorder, and/or condition. In some embodiments, a therapeutically effective amount is administered in a single dose; in some embodiments, multiple unit doses are required to deliver a therapeutically effective amount.

[00128] Treat: As used herein, the term "treat," "treatment," or "treating" refers to any method used to partially or completely alleviate, ameliorate, relieve, inhibit, prevent, delay onset of, reduce severity of, and/or reduce incidence of one or more symptoms or features of a disease, disorder, and/or condition. Treatment may be administered to a subject who does not exhibit signs of a disease, disorder, and/or condition. In some embodiments, treatment may be administered to a subject who exhibits only early signs of the disease, disorder, and/or condition, for example for the purpose of decreasing the risk of developing pathology associated with the disease, disorder, and/or condition.

[00129] Unsaturated: The term "unsaturated," as used herein, means that a moiety has one or more units of unsaturation.

[00130] Wild-type: As used herein, the term "wild-type" has its art-understood meaning that refers to an entity having a structure and/or activity as found in nature in a "normal" (as contrasted with mutant, diseased, altered, etc.) state or context. Those of ordinary skill in the art will appreciate that wild type genes and polypeptides often exist in multiple different forms (e.g., alleles).

[00131] As those skilled in the art will appreciate, methods and compositions described herein relating to provided compounds (e.g., oligonucleotides) generally also apply to pharmaceutically acceptable salts of such compounds.

Description of Certain Embodiments

[00132] Oligonucleotides are useful in various therapeutic, diagnostic, and research applications. For example, PNPLA3 oligonucleotides are useful in therapeutic and research applications, including the treatment of a variety of PNPLA3-associated conditions, disorders, and diseases, including but not limited to non-alcoholic fatty liver disease (NAFLD), also referred to as metabolic dysfunction-associated steatotic liver disease (MASLD), steatosis, non-alcoholic steatohepatitis (NASH), also referred to as metabolic dysfunction-associated steatohepatitis (MASH),cirrhosis, and hepatocellular carcinoma (HCC). Use of naturally occurring nucleic acids is limited, for example, by their susceptibility to endo- and exo-nucleases. As such, various synthetic counterparts have been developed to circumvent these shortcomings and/or to further improve various properties and activities. These include synthetic oligonucleotides that contain chemical modifications, e.g., base modifications, sugar modifications, backbone modifications, etc., which, among other things, render these molecules less susceptible to degradation and improve other properties and/or activities.

[00133] From a structural point of view, modifications to internucleotidic linkages can introduce chirality, and certain properties and activities may be affected by configurations of linkage phosphorus atoms of oligonucleotides. For example, binding affinity, sequence specific binding to complementary RNA, stability to nucleases, activities, delivery, pharmacokinetics, etc. can be affected by, inter alia, chirality of backbone

linkage phosphorus atoms.

[00134] Among other things, the present disclosure utilizes technologies for controlling various structural elements, e.g., sugar modifications and patterns thereof, nucleobase modifications and patterns thereof, modified internucleotidic linkages and patterns thereof, linkage phosphorus stereochemistry and patterns thereof, additional chemical moieties (moieties that are not typically in an oligonucleotide chain) and patterns thereof, etc. With the capability to fully control structural elements of oligonucleotides, the present disclosure provides oligonucleotides with improved and/or new properties and/or activities for various applications, e.g., as therapeutic agents, probes, etc. For example, as demonstrated herein, provided oligonucleotides and compositions thereof are particularly powerful for editing target adenosine in target nucleic acids to, in some embodiments, correct a G to A mutation by converting A to I.

[00135] In some embodiments, an oligonucleotide comprises a sequence that is identical to or is completely or substantially complementary to 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, typically 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 or more, contiguous bases of a PNPLA3 genomic sequence or transcript therefrom (e.g., DNA, pre-mRNA, mRNA, etc.). In some embodiments, a oligonucleotide comprises a sequence that is completely complementary to 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, typically 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 or more, contiguous bases of a PNPLA3 transcript. In some embodiments, a PNPLA3 transcript is a target PNPLA3 transcript comprising one or more target adenosine. In some embodiments, a target PNPLA3 transcript comprises one and no more than one target adenosine. In some embodiments, an oligonucleotide can hybridize with a target PNPLA3 transcript. In some embodiments, such hybridization facilitates modification of A (e.g., conversion of A to I) by, e.g., ADAR1, ADAR2, etc., in a target PNPLA3 transcript.

[00136] In some embodiments, the present disclosure provides a oligonucleotide as disclosed herein, wherein the oligonucleotide has a base sequence which is, or comprises about 10-40, about 15-40, about 20-40, or at least 27, at least 28, at least 29, at least 30, at least 31, at least 32, at least 33, at least 34 contiguous bases of, an oligonucleotide or nucleic acid disclosed herein (e.g., in a Table), or a sequence that is complementary to a target RNA sequence gene, transcript, etc. disclosed herein, and wherein each T can be optionally and independently replaced with U and vice versa. In some embodiments, the present disclosure provides an oligonucleotide or oligonucleotide composition as disclosed herein, e.g., in a Table. In some embodiments, the present disclosure provides a oligonucleotide comprising a base sequence disclosed herein, wherein the oligonucleotide is stereorandom or not chirally controlled, and wherein each T can be optionally and independently replaced with U and vice versa.

[00137] In some embodiments, a oligonucleotide is a single-stranded oligonucleotide for site-directed editing of a nucleoside (e.g., a target adenosine) in a target PNPLA3 nucleic acid, e.g., RNA.

[00138] As described herein, oligonucleotides may contain one or more modified internucleotidic linkages (non-natural phosphate linkages). In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage whose linkage phosphorus is chiral. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, oligonucleotides comprise one or more negatively charged internucleotidic linkages (e.g., phosphorothioate internucleotidic linkages, natural phosphate linkages, etc.). In some embodiments, oligonucleotides comprise one or more non-negatively charged internucleotidic linkages. In some embodiments, oligonucleotides comprise one or more neutral internucleotidic linkages. In some embodiments, the present disclosure provides a oligonucleotide composition wherein the oligonucleotides are stereorandom or not chirally controlled. In some embodiments, a oligonucleotide comprises at least one stereorandom internucleotidic linkage and at least one chirally controlled internucleotidic linkage.

[00139] In some embodiments, oligonucleotides are chirally controlled. In some embodiments, oligonucleotides are chirally pure (or "stereopure", "stereochemically pure"), wherein the oligonucleotide exists as a single stereoisomeric form (in many cases a single diastereoisomeric (or "diastereomeric") form as multiple chiral centers may exist in an oligonucleotide, e.g., at linkage phosphorus, sugar carbon, etc.). As appreciated by those skilled in the art, a chirally pure oligonucleotide is separated from its other stereoisomeric forms (to the extent that some impurities may exist as chemical and biological processes, selectivities and/or purifications etc. rarely, if ever, go to absolute completeness). In a chirally pure oligonucleotide, each chiral center is independently defined with respect to its configuration (for a chirally pure oligonucleotide, each internucleotidic linkage is independently stereodefined or chirally controlled). In contrast to chirally controlled and chirally pure oligonucleotides which comprise stereodefined linkage phosphorus, racemic (or "stereorandom", "non-chirally controlled") oligonucleotides comprising chiral linkage phosphorus, e.g., from traditional phosphoramidite oligonucleotide synthesis without stereochemical control during coupling steps in combination with traditional sulfurization (creating stereorandom phosphorothioate internucleotidic linkages), refer to a random mixture of various stereoisomers (typically diastereoisomers (or "diastereomers") as there are multiple chiral centers in an oligonucleotide; *e.g.*, from traditional oligonucleotide preparation using reagents containing no chiral elements other than those in nucleosides and linkage phosphorus). For example, for A*A*A wherein * is a phosphorothioate internucleotidic linkage (which comprises a chiral linkage phosphorus), a racemic oligonucleotide preparation includes four diastereomers [$2^2 = 4$, considering the two chiral linkage phosphorus, each of which can exist in either of two configurations (*Sp* or *Rp*)]: A *S A *S A, A *S A *R A, A *R A *S A, and A *R A *R A, wherein *S represents a *Sp* phosphorothioate internucleotidic linkage and *R represents a *Rp* phosphorothioate internucleotidic linkage. For a chirally pure oligonucleotide, e.g., A *S A *S A, it exists in a single stereoisomeric form and it is separated from the other stereoisomers (e.g., the diastereomers A *S A *R A, A *R A *S A, and A *R A *R A).

[00140] In some embodiments, oligonucleotides comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more stereorandom internucleotidic linkages (mixture of *Rp* and *Sp* linkage phosphorus at the internucleotidic linkage, e.g., from traditional non-chirally controlled oligonucleotide synthesis). In some embodiments, oligonucleotides comprise one or more (e.g., 1-60, 1-50, 1-40, 1-30, 1-25, 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 or more) chirally controlled internucleotidic linkages (*Rp* or *Sp* linkage phosphorus at the internucleotidic linkage, e.g., from chirally controlled oligonucleotide synthesis). In some embodiments, an internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage is a stereorandom phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage is a chirally controlled phosphorothioate internucleotidic linkage.

[00141] Among other things, the present disclosure provides technologies for preparing chirally controlled (in some embodiments, stereochemically pure) oligonucleotides. In some embodiments, oligonucleotides are stereochemically pure. In some embodiments, oligonucleotides of the present disclosure are about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, or about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% stereochemically pure.

[00142] In some embodiments, the present disclosure provides various oligonucleotide compositions. In some embodiments, oligonucleotide compositions are stereorandom or not chirally controlled. In some embodiments, there are no chirally controlled internucleotidic linkages in oligonucleotides of provided compositions. In some embodiments, internucleotidic linkages of oligonucleotides in compositions comprise one or more chirally controlled internucleotidic linkages (e.g.,, chirally controlled oligonucleotide compositions).

[00143] In some embodiments, a oligonucleotide composition comprises a plurality of oligonucleotides sharing a common base sequence, wherein one or more internucleotidic linkages in the oligonucleotides are chirally controlled and one or more internucleotidic linkages are stereorandom (not chirally controlled). In some embodiments, a oligonucleotide composition comprises a plurality of oligonucleotides sharing a common base sequence, wherein each internucleotidic linkage comprising chiral linkage phosphorus in the oligonucleotides is independently a chirally controlled internucleotidic linkage. In some embodiments, a plurality of oligonucleotides share the same base sequence, and the same base and sugar modification. In some embodiments, a plurality of oligonucleotides share the same base sequence, and the same base, sugar and internucleotidic linkage modification. In some embodiments, a oligonucleotide composition comprises oligonucleotides of the same constitution, wherein one or more internucleotidic linkages are chirally controlled and one or more internucleotidic linkages are stereorandom (not chirally controlled). In some embodiments, a oligonucleotide composition comprises oligonucleotides of the same constitution, wherein each

internucleotidic linkage comprising chiral linkage phosphorus is independently a chirally controlled internucleotidic linkage. In some embodiments, at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90% or 95% of all oligonucleotides, or all oligonucleotides of the common base sequence, are oligonucleotides of the plurality.

[00144] In some embodiments, the present disclosure provides technologies for preparing, assessing and/or utilizing provided oligonucleotides and compositions thereof.

[00145] As used in the present disclosure, in some embodiments, "one or more" is 1-200, 1-150, 1-100, 1-90, 1-80, 1-70, 1-60, 1-50, 1-40, 1-30, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60. In some embodiments, "one or more" is one. In some embodiments, "one or more" is two. In some embodiments, "one or more" is three. In some embodiments, "one or more" is four. In some embodiments, "one or more" is five. In some embodiments, "one or more" is six. In some embodiments, "one or more" is seven. In some embodiments, "one or more" is eight. In some embodiments, "one or more" is nine. In some embodiments, "one or more" is ten. In some embodiments, "one or more" is at least one. In some embodiments, "one or more" is at least two. In some embodiments, "one or more" is at least three. In some embodiments, "one or more" is at least four. In some embodiments, "one or more" is at least five. In some embodiments, "one or more" is at least six. In some embodiments, "one or more" is at least seven. In some embodiments, "one or more" is at least eight. In some embodiments, "one or more" is at least nine. In some embodiments, "one or more" is at least ten.

[00146] As used in the present disclosure, in some embodiments, "at least one" is one or more.

[00147] Various embodiments are described for variables, e.g., R, R^L, L, etc., as examples. Embodiments described for a variable, e.g., R, are generally applicable to all variables that can be such a variable (e.g., R', R", R^L, R^{L1}, etc.).

PNPLA3

[00148] In some embodiments, PNPLA3 refers to a gene or a gene product thereof (including but not limited to a DNA or RNA, a transcript, a protein encoded thereby and can be from any form of PNPLA3, e.g., wild-type or mutant alleles) from any species, which may be known as: PNPLA3, adiponutrin, IPLA2 epsilon, C22orf20, or ADPN. In some embodiments, it refers to the gene and product thereof in a human. In some embodiments, it refers to the gene and product thereof in a non-human primate. Various PNPLA3 sequences, including variants thereof, from human, mouse, rat, monkey, etc. are readily available to those of skill in the art. In some embodiments, PNPLA3 is a human or mouse PNPLA3, which is wild-type or mutant. It has been reported that PNPLA3 can have a number of functions. Various technologies, e.g., assays, cells, animal models, etc. have also been reported and can be utilized for characterization and/or assessment of provided technologies (e.g., oligonucleotides, compositions, methods, etc.) in accordance with the present disclosure.

[00149] In some embodiments, a PNPLA3 gene, transcript (e.g., mRNA or pre-mRNA), or protein variant or isoform comprises a mutation. In some embodiments, a PNPLA3 gene, transcript, or protein is or comprises

a mutation at position corresponding to position 148 of SEQ ID NO: 2. In some embodiments, a PNPLA3 gene, transcript, or protein is or comprises a I148M mutation.

Table A. Example PNPLA3 amino acid sequences.

SEQ ID NO	Description	Sequence
1	Wild-type PNPLA3 amino acid sequence	MYDAERGWSLSFAGCGFLGFYHVGATRCLSEHAPHLLRDA RMLFGASAGALHCVGVLSGIPLEQTLQVLSDLVRKARSRNI GIFHPSFNLSKFLRQGLCKCLPANVHQLISGKIGISLTRVSDGE NVLVSDFRSKDEVVDALVCSCFIPFYSGLIPPSFRGVRYVDG GVSDNVPFIDAKTTITVSPFYGEYDICPKVKSTNFLHVDITKL SLRLCTGNLYLLSRAFVPPDLKVLGEICLRGYLDAFRFLEEK GICNRPQPGLKSSSEGMDPEVAMPSWANMSLDSSPESAALA VRLEGDELLDHLRLSILPWDESILDTLSPRLATALSEEMKDK GGYMSKICNLLPIRIMSYVMLPCTLPVESAIAIVQRLVTWLP DMPDDVLWLQWVTSQVFTRVLMCLLPASRSQMPVSSQQAS PCTPEQDWPCWTPCSPKGCPAETKAEATPRSILRSSLNFFLG NKVPAGAEGLSTFPSFSLEKSL
2	PNPLA3 I148M amino acid sequence	MYDAERGWSLSFAGCGFLGFYHVGATRCLSEHAPHLLRDA RMLFGASAGALHCVGVLSGIPLEQTLQVLSDLVRKARSRNI GIFHPSFNLSKFLRQGLCKCLPANVHQLISGKIGISLTRVSDGE NVLVSDFRSKDEVVDALVCSCFVPFYSGLIPPSFRGVRYVDG GVSDNVPFIDAKTTITVSPFYGEYDICPKVKSTNFLHVDITKL SLRLCTGNLYLLSRAFVPPDLKVLGEICLRGYLDAFRFLEEK GICNRPQPGLKSSSEGMDPEVAMPSWANMSLDSSPESAALA VRLEGDELLDHLRLSILPWDESILDTLSPRLATALSEEMKDK GGYMSKICNLLPIRIMSYVMLPCTLPVESAIAIVQRLVTWLP DMPDDVLWLQWVTSQVFTRVLMCLLPASRSQMPVSSQQAS PCTPEQDWPCWTPCSPKGCPAETKAEATPRSILRSSLNFFLG NKVPAGAEGLSTFPSFSLEKSL

PNPLA3-Associated Conditions, Disorders, or Diseases

[00150] Various conditions, disorders, or diseases are reported to be associated with PNPLA3. Generally, a disease, disorder, or condition is associated with PNPLA3 if the presence, level, activity, and/or form of PNPLA3 and/or products (e.g., transcripts, encoded proteins, etc.) thereof correlates with incidence of and/or susceptibility to the disease, disorder, or condition (e.g., across a relevant population). In some embodiments, a condition, disorder, or disease associated with PNPLA3 may be treated and/or prevented by reducing expression, level, and/or activity of PNPLA3 transcripts and/or proteins. In some embodiments, a condition, disorder, or disease associated with PNPLA3 may be treated and/or prevented by reducing expression, level, and/or activity of mutant PNPLA3 transcripts and/or proteins (e.g., I148M mutant PNPLA3 or variant thereof).

[00151] Various PNPLA3-associated conditions, disorders, or diseases have been reported.

[00152] In some embodiments, a PNPLA3-associated condition, disorder, or disease is non-alcoholic fatty liver disease (NAFLD), also referred to as metabolic dysfunction-associated steatotic liver disease (MASLD) (e.g., hepatic steatosis, NASH, MASH etc.). In some embodiments, a PNPLA3-associated condition, disorder, or disease is cirrhosis. NAFLD / MASLD are reportedly marked by, e.g., the buildup of excess fat in the liver

(Krawczyk et al., Best Pract. Res. Clin. Gastroenterol., 2010). In some embodiments, NAFLD / MASLD comprises nonalcoholic fatty liver (NAFL). NAFL is reportedly marked by, e.g., the buildup of excess fat in the liver, enlargement of the liver, and potential pain. In some embodiments, NAFLD comprises nonalcoholic steatohepatitis (NASH), also referred to as metabolic dysfunction-associated steatohepatitis (MASH). NASH / MASH is reportedly marked by, e.g., the buildup of excess fat in the liver, inflammation of the liver, and potential liver damage. NASH / MASH may also be marked by liver fibrosis (e.g., scarring of the liver) and/or cirrhosis (e.g., scarring, degeneration of liver cells, and/or permanent damage of the liver). Reports indicate that development of NAFLD / MASLD may be associated with risk factors including obesity.

[00153] In some embodiments, a PNPLA3-associated condition, disorder, or disease is cancer. In some embodiments, a PNPLA3-associated condition, disorder, or disease is liver cancer. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hepatocellular carcinoma (HCC). Hepatocellular carcinoma (HCC) is reportedly a type of liver cancer, and further the most common type of liver cancer (Llovet et al., Nat. Rev. Dis. Primers, 2021). In some embodiments, HCC may be associated with chronic liver disease such as alcoholic liver disease, NAFLD, MASLD, NAFL, NASH, MASH, liver fibrosis, and/or liver cirrhosis.

[00154] It has been reported that a SNP (rs738409) in a PNPLA3 gene that results in an I148M mutation in a PNPLA3 protein is associated with the development of various PNPLA3-associated conditions, disorders, or diseases including NAFLD, MASLD, NAFL, NASH, MASH, and HCC (Falleti et al., Liver Int., 2011; Sookoian and Pirola, Hepatology, 2011). In some embodiments, a mutant PNPLA3 transcript comprises a SNP. In some embodiments, a mutant PNPLA3 transcript comprises a SNP corresponding to rs738409. In some embodiments, a PNPLA3 transcript comprises a SNP resulting in a I148M mutation in an encoded PNPLA3 protein.

[00155] In some embodiments, a PNPLA3-associated condition, disorder, or disease is liver fat accumulation. In some embodiments, a PNPLA3-associated condition, disorder, or disease is liver inflammation. In some embodiments, a PNPLA3-associated condition, disorder, or disease is liver fibrosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is liver cirrhosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hyperlipidemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is Type I diabetes. In some embodiments, a PNPLA3-associated condition, disorder, or disease is Type II diabetes mellitus. In some embodiments, a PNPLA3-associated condition, disorder, or disease is idiopathic Type I diabetes (Type Ib). In some embodiments, a PNPLA3-associated condition, disorder, or disease is latent autoimmune diabetes in adults (LADA). In some embodiments, a PNPLA3-associated condition, disorder, or disease is early-onset Type 2 diabetes (EOD). In some embodiments, a PNPLA3-associated condition, disorder, or disease is youth-onset atypical diabetes (YOAD). In some embodiments, a PNPLA3-associated condition, disorder, or disease is maturity onset diabetes of the young (MODY). In some embodiments, a PNPLA3-associated condition, disorder, or disease is malnutrition-related diabetes. In some embodiments, a PNPLA3-associated condition, disorder, or disease is gestational diabetes. In some embodiments, a PNPLA3-associated condition, disorder, or disease is coronary

heart disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is ischemic stroke. In some embodiments, a PNPLA3-associated condition, disorder, or disease is restenosis after angioplasty. In some embodiments, a PNPLA3-associated condition, disorder, or disease is peripheral vascular disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is intermittent claudication. In some embodiments, a PNPLA3-associated condition, disorder, or disease is myocardial infarction. In some embodiments, a PNPLA3-associated condition, disorder, or disease is dyslipidemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is post-prandial lipemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is a impaired glucose tolerance (IGT). In some embodiments, a PNPLA3-associated condition, disorder, or disease is impaired fasting plasma glucose. In some embodiments, a PNPLA3-associated condition, disorder, or disease is metabolic acidosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is ketosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is arthritis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is obesity. In some embodiments, a PNPLA3-associated condition, disorder, or disease is osteoporosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hypertension. congestive heart failure. In some embodiments, a PNPLA3-associated condition, disorder, or disease is left ventricular hypertrophy. In some embodiments, a PNPLA3-associated condition, disorder, or disease is peripheral arterial disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is diabetic retinopathy. In some embodiments, a PNPLA3-associated condition, disorder, or disease is macular degeneration. In some embodiments, a PNPLA3-associated condition, disorder, or disease is cataract. In some embodiments, a PNPLA3-associated condition, disorder, or disease is diabetic nephropathy. In some embodiments, a PNPLA3-associated condition, disorder, or disease is glomerulosclerosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is chronic renal failure. In some embodiments, a PNPLA3-associated condition, disorder, or disease is diabetic neuropathy. In some embodiments, a PNPLA3-associated condition, disorder, or disease is metabolic syndrome. In some embodiments, a PNPLA3-associated condition, disorder, or disease is syndrome X. In some embodiments, a PNPLA3-associated condition, disorder, or disease is premenstrual syndrome. In some embodiments, a PNPLA3-associated condition, disorder, or disease is angina pectoris. In some embodiments, a PNPLA3-associated condition, disorder, or disease is thrombosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is atherosclerosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is transient ischemic attacks. In some embodiments, a PNPLA3-associated condition, disorder, or disease is stroke. vascular restenosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hyperglycemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hyperinsulinemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hypertriglyceridemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is insulin resistance. In some embodiments, a PNPLA3-associated condition, disorder, or disease is impaired glucose metabolism. In some embodiments, a PNPLA3-associated condition, disorder, or disease is erectile dysfunction. In some embodiments, a PNPLA3-associated condition, disorder, or disease is a skin and

connective tissue disorder. In some embodiments, a PNPLA3-associated condition, disorder, or disease is a foot ulceration. In some embodiments, a PNPLA3-associated condition, disorder, or disease is ulcerative colitis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is endothelial dysfunction. In some embodiments, a PNPLA3-associated condition, disorder, or disease is impaired vascular compliance. In some embodiments, a PNPLA3-associated condition, disorder, or disease is hyper apo B lipoproteinemia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is Alzheimer's disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is schizophrenia. In some embodiments, a PNPLA3-associated condition, disorder, or disease is impaired cognition. In some embodiments, a PNPLA3-associated condition, disorder, or disease is inflammatory bowel disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is Crohn's disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is irritable bowel syndrome. In some embodiments, a PNPLA3-associated condition, disorder, or disease is alcoholic liver disease. In some embodiments, a PNPLA3-associated condition, disorder, or disease is alcoholic steatosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is steatosis. In some embodiments, a PNPLA3-associated condition, disorder, or disease is alcoholic cirrhosis.

[00156] Among other things, provided technologies are useful for treating or preventing a condition, disorder, or disease associated with PNPLA3, e.g., non-alcoholic fatty liver disease (NAFLD), also referred to as metabolic dysfunction-associated steatotic liver disease (MASLD) (e.g., hepatic steatosis, NASH / MASH, etc.), cirrhosis, hepatocellular carcinoma (HCC), etc.

[00157] In some embodiments, provide technologies may be used to treat NAFLD / MASLD. In some embodiments, treatment comprises administration of an oligonucleotide or composition disclosed herein. In some embodiments, treatment comprises reduction of reduction of signs and/or symptoms associated with NAFLD / MASLD (e.g., fatigue, abdominal swelling, shortness of breath, edema, itchy skin, ascites, enlarged spleen, red palms, jaundice, etc.).

[00158] In some embodiments, provide technologies may be used to treat cirrhosis. In some embodiments, treatment comprises administration of an oligonucleotide or composition disclosed herein. In some embodiments, treatment comprises reduction of reduction of signs and/or symptoms associated with cirrhosis (e.g., fatigue, loss of appetite, nausea, edema, weight loss, itchy skin, jaundice, ascites, red palms, etc.).

[00159] In some embodiments, provided technologies (e.g., oligonucleotides, compositions, methods, etc.) reduce expression, level functions, and/or activities of mutant PNPLA3 transcripts (e.g., I148M PNPLA3 mutant) and proteins encoded thereby. In some embodiments, such reduction further comprises increased levels of alternative PNPLA3 transcripts (e.g., I148V PNPLA3) that encodes a PNPLA3 protein with improved lipase activity. In some embodiments, such alternative PNPLA3 transcripts and proteins encoded thereby can reduce symptoms or characteristics of one or more PNPLA3-associated conditions, disorders, or diseases.

[00160] In some embodiments, the present disclosure provides methods for reducing a level, function, and/or activity of mutant PNPLA3 transcripts (e.g., I148M PNPLA3 mutant), comprising contacting the

mutant PNPLA3 transcript with an oligonucleotide or a composition of the present disclosure. In some embodiments, such reduction further comprises increased levels of alternative PNPLA3 transcripts (e.g., I148V PNPLA3) that encodes a PNPLA3 protein with improved lipase activity.

[00161] In some embodiments, treatment or prevention with provided technologies increases lipase activity of a PNPLA3 protein, through reducing level of mutant PNPLA3 transcripts (e.g., I148M PNPLA3 mutant) and increasing levels of alternative PNPLA3 transcripts (e.g., I148V PNPLA3) that encodes a PNPLA3 protein with improved lipase activity. In some embodiments, treatment or prevention with provided technologies reduces the rate of clinical decline, or delays or prevents onset of a condition, disorder, or disease.

[00162] As appreciated by those skilled in the art, mechanisms, genotypes, symptoms, biomarkers, etc. of such conditions, disorders, or diseases may be utilized in accordance with the present disclosure to characterize/assess provided technologies.

[00163] In some embodiments, a condition, disease or disorder is associated with I148M mutation in PNPLA3. In some embodiments, a subject is homozygous with respect to I148M mutation in PNPLA3. In some embodiments, a condition, disease or disorder is less associated with I148V in PNPLA3 compared to I148M in PNPLA3.

[00164] Among other things, the present disclosure encompasses the recognition that I148M mutation in PNPLA3 increases risks for various conditions, diseases or disorders. For example, homozygous I148M patients can have significantly higher risk of HCC which can be liver-related. In some embodiments, PNPLA3 knockdown or knockout may result in worse conditions compared to PNPLA3-I148M homozygous and heterozygous genotypes (e.g., increased steatosis, increased lipid accumulation, increased susceptibility to ethanol and methotrexate toxicity, etc.). In some embodiments, the present disclosure encompasses the recognition that conversion of I148M to I148V (e.g., via genome DNA editing, RNA editing, etc.) in PNPLA3 can provide various benefits and advantages compared to reference technologies (e.g., knockdown, knockout, etc.). In some embodiments, provided technologies increases or restores certain PNPLA3 functions. In some embodiments, provided technologies increases or restores certain PNPLA3 activities, e.g., lipase activity. In some embodiments, provided technologies can reduce levels of various markers, e.g., triglyceride. In some embodiments, provided technologies reduce triglyceride level in liver which has been reported to be associated with liver PNPLA3 abundance.

Oligonucleotides

[00165] Among other things, the present disclosure provides PNPLA3 oligonucleotides of various designs, which may comprise various nucleobases and patterns thereof, sugars and patterns thereof, internucleotidic linkages and patterns thereof, and/or additional chemical moieties and patterns thereof as described in the present disclosure. In some embodiments, provided oligonucleotides can direct A to I editing in target PNPLA3 transcripts. In some embodiments, oligonucleotides of the present disclosure are single-stranded oligonucleotides capable of site-directed editing of an adenosine (conversion of A into I) in a target PNPLA3 RNA sequence.

[00166] In some embodiments, oligonucleotides are of suitable lengths and sequence complementarity to specifically hybridize with target PNPLA3 transcripts. In some embodiments, oligonucleotides are sufficiently long and are sufficiently complementary to target PNPLA3 transcripts to distinguish target PNPLA3 transcripts from other nucleic acids to reduce off-target effects. In some embodiments, oligonucleotides are sufficiently short to facilitate delivery, reduce manufacture complexity and/or cost which maintaining desired properties and activities (e.g., editing of adenosine).

[00167] In some embodiments, a oligonucleotide has a length of about 10-200 (e.g., about 10-20, 10-30, 10-40, 10-50, 10-60, 10-70, 10-80, 10-90, 10-100, 10-120, 10-150, 20-30, 20-40, 20-50, 20-60, 20-70, 20-80, 20-90, 20-100, 20-120, 20-150, 20-200, 25-30, 25-40, 25-50, 25-60, 25-70, 25-80, 25-90, 25-100, 25-120, 25-150, 25-200, 30-40, 30-50, 30-60, 30-70, 30-80, 30-90, 30-100, 30-120, 30-150, 30-200, 10, 20, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 60, etc.) nucleobases. In some embodiments, the base sequence of a oligonucleotide is about 10-60 nucleobases in length. In some embodiments, a base sequence is about 15-50 nucleobases in length. In some embodiments, a base sequence is from about 15 to about 35 nucleobases in length. In some embodiments, a base sequence is from about 25 to about 34 nucleobases in length. In some embodiments, a base sequence is from about 26 to about 35 nucleobases in length. In some embodiments, a base sequence is from about 27 to about 32 nucleobases in length. In some embodiments, a base sequence is from about 29 to about 35 nucleobases in length. In some embodiments, a base sequence is about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60 nucleobases in length. In some other embodiments, a base sequence is or is at least 35 nucleobases in length. In some other embodiments, a base sequence is or is at least 34 nucleobases in length. In some other embodiments, a base sequence is or is at least 33 nucleobases in length. In some other embodiments, a base sequence is or is at least 32 nucleobases in length. In some other embodiments, a base sequence is or is at least 31 nucleobases in length. In some other embodiments, a base sequence is or is at least 30 nucleobases in length. In some other embodiments, a base sequence is or is at least 29 nucleobases in length. In some other embodiments, a base sequence is or is at least 28 nucleobases in length. In some other embodiments, a base sequence is or is at least 27 nucleobases in length. In some other embodiments, a base sequence is or is at least 26 nucleobases in length. In some other embodiments, the base sequence of the complementary portion in a duplex is at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 16, 27, 28, 29, 30, 31, 32, 33, 34, 35 or more nucleobases in length. In some other embodiments, it is at least 18 nucleobases in length. In some other embodiments, it is at least 19 nucleobases in length. In some other embodiments, it is at least 20 nucleobases in length. In some other embodiments, it is at least 21 nucleobases in length. In some other embodiments, it is at least 22 nucleobases in length. In some other embodiments, it is at least 23 nucleobases in length. In some other embodiments, it is at least 24 nucleobases in length. In some other embodiments, it is at least 25 nucleobases in length. Among other things, the present disclosure provides oligonucleotides of comparable or better properties and/or comparable or higher activities but of shorter lengths compared to prior reported adenosine editing

oligonucleotides.

[00168] In some embodiments, a base sequence of an oligonucleotide is complementary to a base sequence of a target PNPLA3 transcript (e.g., complementarity to a portion of the target nucleic acid comprising the target adenosine) with 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches which are not Watson-Crick base pairs (AT, AU and CG). In some embodiments, there are no mismatches. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches. In some embodiments, there are 10 mismatches. In some embodiments, oligonucleotides may contain portions that are not designed for complementarity (e.g., loops, protein binding sequences, etc., for recruiting of proteins, e.g., ADAR). As those skilled in the art will appreciate, when calculating mismatches and/or complementarity, such portions may be properly excluded. In some embodiments, complementarity, e.g., between oligonucleotides and target nucleic acids, is about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.). In some embodiments, complementarity is at least about 60%. In some embodiments, complementarity is at least about 65%. In some embodiments, complementarity is at least about 70%. In some embodiments, complementarity is at least about 75%. In some embodiments, complementarity is at least about 80%. In some embodiments, complementarity is at least about 85%. In some embodiments, complementarity is at least about 90%. In some embodiments, complementarity is at least about 95%. In some embodiments, complementarity is 100% across the length of an oligonucleotide. In some embodiments, complementarity is 100% except at a nucleoside opposite to a target nucleoside (e.g., adenosine) across the length of an oligonucleotide. Typically, complementarity is based on Watson-Crick base pairs AT, AU and CG. Those skilled in the art will appreciate that when assessing complementarity of two sequences of different lengths (e.g., a provided oligonucleotide and a target nucleic acid) complementarity may be properly based on the length of the shorter sequence and/or maximum complementarity between the two sequences. In many embodiments, oligonucleotides and target nucleic acids are of sufficient complementarity such that modifications are selectively directed to target adenosine sites.

[00169] In some embodiments, one or more mismatches are independently wobbles. In some embodiments, each mismatch is a wobble. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles. In some embodiments, the number

is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5. In some embodiments, a wobble is G-U, I-A, G-A, I-U, I-C, I-T, A-A, or reverse A-T. In some embodiments, a wobble is G-U, I-A, G-A, I-U, or I-C. In some embodiments, I-C may be considered a match when I is a 3' immediate nucleoside next to a nucleoside opposite to a target nucleoside. In some embodiments, a base that forms a wobble pair (e.g., U which can form a G-U wobble) may replace a base that forms a match pair (e.g., C which matches G) and can provide a oligonucleotide with editing activity.

[00170] In some embodiments, N_9 produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_9 produces a G-U wobble base pairing aligned with a target nucleic acid. In some embodiments, N_9 produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_9 is optionally substituted C and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_9 is optionally substituted U and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a 16th nucleoside from the 5'-end of an oligonucleotide produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of a 16th nucleoside from the 5'-end of an oligonucleotide is C. In some embodiments, a nucleobase of a 16th nucleoside from the 5'-end of an oligonucleotide is U. In some embodiments, N_{16} produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{16} produces a G-U wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_{16} is U. In some embodiments, a 9th nucleoside from the 5'-end of an oligonucleotide produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a 9th nucleoside from the 5'-end of an oligonucleotide produces a G-U wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of a 9th nucleoside from the 5'-end of an oligonucleotide is U. In some embodiments, N_{16} produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_{16} is optionally substituted A and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a 9th nucleoside from the 5'-end of an oligonucleotide produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of a 9th nucleoside from the 5'-end of an oligonucleotide is A. In some embodiments, N_{20} produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{20} produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_{20} is optionally substituted T and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_{20} is optionally substituted U and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of N_{20} is optionally substituted C and produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a 5th nucleoside from the 5'-end of an oligonucleotide produces a mismatch

or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a 5th nucleoside from the 5'-end of an oligonucleotide produces a mismatch when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, a nucleobase of a 5th nucleoside from the 5'-end of an oligonucleotide is T. In some embodiments, a nucleobase of a 5th nucleoside from the 5'-end of an oligonucleotide is U. In some embodiments, a nucleobase of a 5th nucleoside from the 5'-end of an oligonucleotide is A. In some embodiments, a nucleobase of a 5th nucleoside from the 5'-end of an oligonucleotide is C.

[00171] In some embodiments, oligonucleotides comprise multiple mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise two or more mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise three or more mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise four or more mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise five or more mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise two mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise three mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise four mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, oligonucleotides comprise five mismatches and/or wobble-base pairings when aligned with a target nucleic acid. In some embodiments, N_{21} and N_{20} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{20} and N_{19} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{19} and N_{18} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{18} and N_{17} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{17} and N_{16} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{16} and N_{15} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{15} and N_{14} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{14} and N_{13} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{13} and N_{12} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{12} and N_{11} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{11} and N_{10} produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_{10} and N_9 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_9 and N_8

produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_8 and N_7 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_7 and N_6 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_6 and N_5 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_5 and N_4 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_4 and N_3 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid. In some embodiments, N_3 and N_2 produce mismatches and/or wobble-base pairings when the oligonucleotide is aligned with a target nucleic acid.

[00172] In some embodiments, duplexes of oligonucleotides and target PNPLA3 transcripts comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00173] In some embodiments, distances between two mismatches, mismatches and one or both ends of oligonucleotides (or a portion thereof, e.g., first domain, second domain, first subdomain, second subdomain, third subdomain), and/or mismatches and nucleosides opposite to target adenosine can independently be 0-50, 0-40, 0-30, 0-25, 0-20, 0-15, 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, or 35 nucleobases (not including mismatches, end nucleosides and nucleosides opposite to target adenosine). In some embodiments, a number is 0-30. In some embodiments, a number is 0-20. In some embodiments, a number is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20. In some embodiments, a distance between two mismatches is 0-20. In some embodiments, a distance between two mismatches is 1-10. In some embodiments, a distance between a mismatch and a 5'-end nucleoside of an oligonucleotide is 0-20. In some embodiments, a distance between a mismatch and a 5'-end nucleoside of an oligonucleotide is 5-20. In some embodiments, a distance between a mismatch and a 3'-end nucleoside of an oligonucleotide is 0-40. In some embodiments, a distance between a mismatch and a 3'-end nucleoside of an oligonucleotide is 5-20. In some embodiments, a distance between a mismatch and a nucleoside opposite to a target adenosine is 0-20. In some embodiments, a distance between a mismatch and a nucleoside opposite to a target adenosine is 1-10. In some embodiments, the number of nucleobases for a distance is 0. In some embodiments, it is 1. In some embodiments, it is 2. In some embodiments, it is 3. In some embodiments, it is 4. In some embodiments, it is 5. In some embodiments, it is 6. In some embodiments, it is 7. In some embodiments, it is 8. In some

embodiments, it is 9. In some embodiments, it is 10. In some embodiments, it is 11. In some embodiments, it is 12. In some embodiments, it is 13. In some embodiments, it is 14. In some embodiments, it is 15. In some embodiments, it is 16. In some embodiments, it is 17. In some embodiments, it is 18. In some embodiments, it is 19. In some embodiments, it is 20. In some embodiments, a mismatch is at an end, e.g., a 5'-end or 3'-end of a first domain, second domain, first subdomain, second subdomain, or third subdomain. In some embodiments, a mismatch is at a nucleoside opposite to a target adenosine.

[00174] In some embodiments, provided oligonucleotides can direct adenosine editing (e.g.,, converting A to I) in a target PNPLA3 transcript and have a base sequence which consists of, comprises, or comprises a portion (e.g., a span of 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more contiguous bases) of the base sequence of a oligonucleotide disclosed herein, wherein each T can be independently replaced with U and vice versa, and the oligonucleotide comprises at least one non-naturally-occurring modification of a base, sugar and/or internucleotidic linkage.

[00175] In some embodiments, a provided oligonucleotide comprises one or more carbohydrate moieties. In some embodiments, a provided oligonucleotide comprises one or more GalNAc moieties. In some embodiments, a provided oligonucleotide comprises one or more targeting moieties. Non-limiting examples of such additional chemical moieties which can be conjugated to oligonucleotide chain are described herein.

[00176] In some embodiments, provided PNPLA3 oligonucleotides can direct a modification of an A in a in a target PNPLA3 transcript, wherein the A is in the same codon as a C to G mutation. In some embodiments, a modification of an A in a PNPLA3 transcript is or comprises conversion of A to I, which can be read as G during translation or other biological processes. In some embodiments, modification of an A in a PNPLA3 transcript, e.g., RNA transcript, produces produce an alternative amino acid codon. In some embodiments, provided oligonucleotides can direct a modification of an A in a target PNPLA3 transcript or a product thereof via ADAR-mediated deamination. In some embodiments, provided oligonucleotides can direct a modification of an A in a target PNPLA3 transcript or a product thereof via ADAR-mediated deamination by recruiting an endogenous ADAR (e.g., in a target cell) and facilitating the ADAR-mediated deamination. Regardless, however, the present disclosure is not limited to any particular mechanism. In some embodiments, the present disclosure provides oligonucleotides, compositions, methods, etc., capable of operating via double-stranded RNA interference, single-stranded RNA interference, RNase H-mediated knock-down, steric hindrance of translation, ADAR-mediated deamination or a combination of two or more such mechanisms.

[00177] In some embodiments, an oligonucleotide comprises a structural element or a portion thereof described herein, e.g., in a Table. In some embodiments, a oligonucleotide has a base sequence which comprises the base sequence (or a portion thereof) wherein each T can be independently substituted with U, pattern of chemical modifications (or a portion thereof), and/or a format of an oligonucleotide disclosed herein, e.g., in a Table or in the Figures, or otherwise disclosed herein.

[00178] Among other things, provided oligonucleotides may hybridize to their target PNPLA3 nucleic acids (e.g., pre-mRNA, mature mRNA, etc.). In some embodiments, oligonucleotide can hybridize to a target

PNPLA3 RNA sequence nucleic acid in any stage of RNA processing, including but not limited to a pre-mRNA or a mature mRNA. In some embodiments, an oligonucleotide can hybridize to any element of a target PNPLA3 nucleic acid or its complement, including but not limited to: a promoter region, an enhancer region, a transcriptional stop region, a translational start signal, a translation stop signal, a coding region, a non-coding region, an exon, an intron, an intron/exon or exon/intron junction, the 5' UTR, or the 3' UTR.

[00179] In some embodiments, oligonucleotide hybridizes to two or more variants of transcripts derived from a sense strand of a target site (e.g., a target PNPLA3 sequence).

[00180] In some embodiments, provided oligonucleotides contain increased levels of one or more isotopes. In some embodiments, provided oligonucleotides are labeled, e.g., by one or more isotopes of one or more elements, e.g., hydrogen, carbon, nitrogen, etc. In some embodiments, provided oligonucleotides in provided compositions, e.g., oligonucleotides of a plurality of a composition, comprise base modifications, sugar modifications, and/or internucleotidic linkage modifications, wherein the oligonucleotides contain an enriched level of deuterium. In some embodiments, provided oligonucleotides are labeled with deuterium (replacing $-^{1}H$ with $-^{2}H$) at one or more positions. In some embodiments, one or more ^{1}H of an oligonucleotide chain or any moiety conjugated to the oligonucleotide chain (e.g., a targeting moiety, etc.) is substituted with ^{2}H. Such oligonucleotides can be used in compositions and methods described herein.

[00181] In some embodiments, oligonucleotides comprise one or more modified nucleobases, one or more modified sugars, and/or one or more modified internucleotidic linkages as described herein. In some embodiments, oligonucleotides comprise a certain level of modified nucleobases, modified sugars, and/or modified internucleotidic linkages, e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all nucleobases, sugars, and internucleotidic linkages, respectively, within an oligonucleotide.

[00182] In some embodiments, oligonucleotides comprise one or more modified sugars. In some embodiments, an oligonucleotide comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars. In some embodiments, an oligonucleotide comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars with 2'-F modification. In some embodiments, an oligonucleotide comprises about 2-50 (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15,

16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., 2-40, 2-30, 2-25, 2-20, 2-15, 2-10, 3-40, 3-30, 3-25, 3-20, 3-15, 3-10, 4-40, 4-30, 4-25, 4-20, 4-15, 4-10, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 6-40, 6-30, 6-25, 6-20, 6-15, 6-10, 7-40, 7-30, 7-25, 7-20, 7-15, 7-10, 8-40, 8-30, 8-25, 8-20, 8-15, 8-10, 9-40, 9-30, 9-25, 9-20, 9-15, 9-10, 10-40, 10-30, 10-25, 10-20, 10-15, about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) consecutive modified sugars with 2'-F modification. In some embodiments, an oligonucleotide comprises 2 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 3 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 4 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 5 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 6 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 7 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 8 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 9 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises 10 consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises two or more 2'-F modified sugar blocks, wherein each sugar in a 2'-F modified sugar block is independently a 2'-F modified sugar. In some embodiments, each 2'-F modified sugar block independently comprises or consists of 2, 3, 4, 5, 6, 7, 8, 9, or 10 consecutive 2'-F modified sugars as described herein. In some embodiments, two consecutive 2'-F modified sugar blocks are independently separated by a separating block which separating block comprises one or more sugars that are independently not 2'-F modified sugars. In some embodiments, an oligonucleotide comprises one or more (e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) 2'-F blocks and one or more (e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) separating blocks. In some embodiments, a first domain comprises one or more (e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) 2'-F blocks and one or more (e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) separating blocks. In some embodiments, each first domain block bonded to a first domain 2'-F block is a separating block. In some embodiments, each first domain block bonded to a first domain separating block is a first domain 2'-F block. In some embodiments, each sugar in a separating block is independently not 2'-F modified. In some embodiments, two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) or all sugars in a separating block are independently not 2'-F modified. In some embodiments, a separating block comprises one or more bicyclic sugars (e.g., LNA sugar, cEt sugar, etc.) and/or one or more 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, a separating block comprises one or more 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, two or more non-2'-F modified sugars are consecutive. In some embodiments, two or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.) are consecutive. In some embodiments, a separating block comprises two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OR modified sugars wherein R is

optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, a separating block comprises two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) consecutive 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE sugar. In some embodiments, a separating block comprises one or more 2'-F modified sugars. In some embodiments, none of 2'-F modified sugars in a separating block are next to each other. In some embodiments, a separating block contain no 2'-F modified sugars. In some embodiments, each sugar in a separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each sugar in each separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each sugar in a separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in each separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a separating block is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in each separating block is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in a separating block is independently a 2'-OMe modified sugar. In some embodiments, each sugar in a separating block is independently a 2'-MOE modified sugar. In some embodiments, a separating block comprises a 2'-OMe sugar and 2'-MOE modified sugar. In some embodiments, each 2'-F block and each separating block independently contains 1, 2, 3, 4, or 5 nucleosides. In some embodiments, each 2'-F block and each separating block independently contains 1, 2, or 3 nucleosides.

[00183] In some embodiments, one or more sugars of N_{21}, N_{20}, N_{18}, N_{16}, N_{15}, N_{14}, N_{13}, N_{12}, N_{10}, N_9, N_8, N_7, N_6, N_5, N_4, N_3, N_2, and N_{-3} are independently a 2'-F modified sugar. In some embodiments, one or more sugars of N_{21} and N_{20} are independently a 2'-F modified sugar. In some embodiments, one or more sugars of N_{18}, N_{16}, N_{15}, N_{14}, N_{13}, and N_{12} are independently a 2'-F modified sugar. In some embodiments, one or more sugars of N_{10}, N_9, N_8, N_7, N_6, N_5, N_4, N_3, and N_2 are independently a 2'-F modified sugar.

[00184] In some embodiments, a sugar of N_{16} is a 2'-F modified sugar. In some embodiments, a sugar of a 9th nucleoside from the 5'-end of an oligonucleotide is a 2'-F modified sugar. In some embodiments, a sugar of N_{15} is a 2'-F modified sugar. In some embodiments, a sugar of a 10th nucleoside from the 5'-end of an oligonucleotide is a 2'-F modified sugar.

[00185] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are modified sugars. In some embodiments, about 10%-100%, 20-100%, 30%-

100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are modified sugars independently selected from 2'-F modified sugars, 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic, and bicyclic sugars (e.g., LNA sugars, cEt sugars, etc.). In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%.

[00186] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are modified sugars independently selected from 2'-F modified sugars and 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are modified sugars independently selected from 2'-F modified sugars, 2'-OMe modified sugars and 2'-MOE modified sugars. In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%.

[00187] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are modified sugars independently selected from 2'-F modified sugars and 2'-OMe

modified sugars. In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%.

[00188] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-F modified sugars. In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%. In some embodiments, 10 or more (e.g., about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, 10-50, 10-40, 10-30, 10-25, 15-50, 15-40, 15-30, 15-25, 20-50, 20-40, 20-30, 20-25, etc.) sugars are 2'-F modified sugars. In some embodiments, an oligonucleotide comprises two or more (e.g., 2-30, 2-25, 2-20, 2-15, 3-10, 3-30, 3-25, 3-20, 3-15, 3-10, 4-30, 4-25, 4-20, 4-15, 4-10, 5-30, 5-25, 5-20, 5-15, 5-10, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises one or more 2'-F blocks each independently comprising two or more (e.g., 2-30, 2-25, 2-20, 2-15, 3-10, 3-30, 3-25, 3-20, 3-15, 3-10, 4-30, 4-25, 4-20, 4-15, 4-10, 5-30, 5-25, 5-20, 5-15, 5-10, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) consecutive 2'-F modified sugars. In some embodiments, an oligonucleotide comprises two or more 2'-F blocks as described herein separated by one or more separating blocks as described herein. In some embodiments, a 2'-F block has 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-F modified sugars. In some embodiments, a 2'-F block has no more than 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 10 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 9 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 8 2'-F modified sugars. In some embodiments, each sugar in

each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 7 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 6 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 5 2'-F modified sugars. In some embodiments, each sugar in each 2'-F blocks is a 2'-F modified sugar, and each 2'-F block independently has no more than 4 2'-F modified sugars. In some embodiments, each block bonded to a 2'-F block is independently a block that comprises no 2'-F modified sugar. In some embodiments, each block bonded to a 2'-F block is independently a block that comprises a natural DNA or RNA sugar, a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each block bonded to a 2'-F block is independently a block that comprises a natural DNA or RNA sugar, a 2'-OMe modified sugar, 2'-MOE modified sugar or a bicyclic sugar. In some embodiments, each block bonded to a 2'-F block is independently a block that comprises a natural DNA or RNA sugar, a 2'-OMe modified sugar or 2'-MOE modified sugar. In some embodiments, each nucleoside in a first domain bonded to a 2'-F block in a first domain is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each nucleoside in a first domain bonded to a 2'-F block in a first domain is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each nucleoside in a first domain bonded to a 2'-F block in a first domain is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each nucleoside in a second domain bonded to a 2'-F block in a second domain is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each nucleoside in a second domain bonded to a 2'-F block in a second domain is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each nucleoside in a second domain bonded to a 2'-F block in a second domain is independently a 2'-OMe or 2'-MOE modified sugar.

[00189] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-OMe or 2'-MOE modified sugars. In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a

percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%.

[00190] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-OMe modified sugars. In some embodiments, a percentage is about or at least about 30%. In some embodiments, a percentage is about or at least about 40%. In some embodiments, a percentage is about or at least about 50%. In some embodiments, a percentage is about or at least about 60%. In some embodiments, a percentage is about or at least about 70%. In some embodiments, a percentage is about or at least about 80%. In some embodiments, a percentage is about or at least about 90%. In some embodiments, a percentage is about or at least about 95%.

[00191] In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars are 2'-MOE modified sugars.

[00192] In some embodiments, sugars of the first (5'-end) one or several (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, etc.) and/or the last (3'-end) one or several (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, etc.) nucleosides are independently modified sugars. In some embodiments, the first one or several sugars are independently modified sugars. In some embodiments, the last one or several sugars are independently modified sugars. In some embodiments, both the first and last one or several sugars are independently modified sugars. In some embodiments, modified sugars are independently non-2'-F modified sugars, e.g., bicyclic sugars, 2'-OR modified sugars wherein R is as described herein and is not −H (e.g., optionally substituted C_{1-6} aliphatic). In

some embodiments, they are independently selected from bicyclic sugars and 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, they are independently 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, they are independently 2'-OMe modified sugars and 2'-MOE modified sugars. In some embodiments, the first several sugars comprises one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic or bicyclic sugars (e.g., LNA, cEt, etc.) as described herein. In some embodiments, the first several sugars comprises one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the first several sugars comprises one or more 2'-OMe modified sugars. In some embodiments, the first several sugars comprises one or more 2'-MOE modified sugars. In some embodiments, the first several sugars comprises one or more 2'-OMe modified sugars and one or more 2'-MOE modified sugars. In some embodiments, the last several sugars comprises one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic or bicyclic sugars (e.g., LNA, cEt, etc.) as described herein. In some embodiments, the last several sugars comprises one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the last several sugars comprises one or more 2'-OMe modified sugars. In some embodiments, the last several sugars comprises one or more 2'-MOE modified sugars. In some embodiments, the last several sugars comprises one or more 2'-OMe modified sugars and one or more 2'-MOE modified sugars. In some embodiments, the last several sugars are independently 2'-OMe modified sugars. In some embodiments, the first several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive bicyclic sugars or 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the first several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the first several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive modified sugars wherein each modified sugar is independently a 2'-OMe modified sugar or a 2'-MOE modified sugar. In some embodiments, the first several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-OMe modified sugars. In some embodiments, the first several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-MOE modified sugars. In some embodiments, the last several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the last several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive modified sugars wherein each modified sugar is independently a 2'-OMe modified sugar or a 2'-MOE modified sugar. In some embodiments, the last several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-OMe modified sugars. In some embodiments, the last several sugars comprise three or more consecutive 2'-OMe modified sugars. In some embodiments, the last several sugars comprise four or more consecutive 2'-OMe modified sugars. In some embodiments, the last several sugars comprise five or more consecutive 2'-OMe modified sugars. In some embodiments, the last several sugars comprise six or more consecutive 2'-OMe modified sugars. In some embodiments, the last several sugars comprise two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) consecutive 2'-MOE modified

sugars.

[00193] In some embodiments, one or more (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of the first several (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) sugars are modified sugars. In some embodiments, one or more (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of the first several (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar (e.g., a sugar comprising 2'–O–CH_2–4', wherein the –CH_2– is optionally substituted (e.g., a LNA sugar, a cET sugar (e.g., (S)-cEt))). In some embodiments, two or more of the first several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, three or more of the first several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, four or more of the first several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, the one or more sugars are consecutive. In some embodiments, the first one, two, three or four sugars are modified sugars. In some embodiments, the first two sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, the first three sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, the first four sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each bicyclic sugar is independently a LNA sugar or a cEt sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the first several sugars, or the first several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the first several sugars, or the first several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the first several sugars, or the first several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OMe modified sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the first several sugars, or the first several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-MOE modified sugar. In some embodiments, the first one, two, three, four or more sugars are independently 2'-OMe modified sugars. In some embodiments, the first sugar is a 2'-OMe modified sugar. In some embodiments, the first two sugars are independently 2'-OMe modified sugars. In some embodiments, the first three sugars are independently 2'-OMe modified sugars. In some embodiments, the first four sugars are independently 2'-OMe modified sugars. In some embodiments, the first one, two, three, four or more sugars are independently 2'-MOE modified sugars. In some embodiments, the first sugar is a 2'-MOE modified sugar. In some embodiments, the first two sugars are independently 2'-MOE modified sugars. In some embodiments, the first three sugars are independently 2'-MOE modified sugars. In some

embodiments, the first four sugars are independently 2'-MOE modified sugars. In some embodiments, each of such modified sugars is independently the sugar of a nucleoside whose nucleobase is optionally substituted or protected A, T, C, G, or U, or an optionally substituted or protected tautomer of A, T, C, G, or U. In some embodiments, one or more such sugars are independently bonded to a non-negatively charged internucleotidic linkage. In some embodiments, one or more such sugars are independently bonded to a neutral internucleotidic linkage such as n001. In some embodiments, a non-negatively charged internucleotidic linkage or neutral internucleotidic linkage, e.g., n001, is chirally controlled. In some embodiments, it is *Rp*. In some embodiments, one or more such sugars are independently bonded to a phosphorothioate internucleotidic linkage. In some embodiments, a phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, it is *Sp*. In some embodiments, as described herein, the internucleotidic linkage between the first and second nucleosides is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n025. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, it is chirally controlled. In some embodiments, it is *Rp*. In some embodiments, except the internucleotidic linkage between the first and second nucleosides, each internucleotidic linkages bonded to nucleosides comprising the one or more of the first several, or the first several modified sugars are independently phosphorothioate internucleotidic linkages. In some embodiments, each is chirally controlled. In some embodiments, each is *Sp*. In some embodiments, a first nucleoside is connected to an additional moiety, e.g., Mod001, optionally through a linker, e.g., L001, through its 5'-end carbon (in some embodiments, via a phosphate group).

[00194] In some embodiments, one or more (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of the last several (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) sugars are modified sugars. In some embodiments, one or more (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of the last several (1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar (e.g., a sugar comprising 2'–O–CH_2–4', wherein the –CH_2– is optionally substituted (e.g., a LNA sugar, a cET sugar (e.g., (S)-cEt))). In some embodiments, two or more of the last several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, three or more of the last several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, four or more of the last several sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, the one or more sugars are consecutive. In some embodiments, the last one, two, three or four sugars are modified sugars. In some embodiments, the last two sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, the last three sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a

bicyclic sugar. In some embodiments, the last four sugars are modified sugars each independently selected from a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic and a bicyclic sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each bicyclic sugar is independently a LNA sugar or a cEt sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the last several sugars, or the last several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the last several sugars, or the last several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the last several sugars, or the last several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-OMe modified sugar. In some embodiments, each of the one or more (e.g., 1, 2, 3, 4, or 5) sugars of the last several sugars, or the last several (e.g., 1, 2, 3, 4, or 5) sugar(s), is independently a 2'-MOE modified sugar. In some embodiments, the last one, two, three, four or more sugars are independently 2'-OMe modified sugars. In some embodiments, the last sugar is a 2'-OMe modified sugar. In some embodiments, the last two sugars are independently 2'-OMe modified sugars. In some embodiments, the last three sugars are independently 2'-OMe modified sugars. In some embodiments, the last four sugars are independently 2'-OMe modified sugars. In some embodiments, the last one, two, three, four or more sugars are independently 2'-MOE modified sugars. In some embodiments, the last sugar is a 2'-MOE modified sugar. In some embodiments, the last two sugars are independently 2'-MOE modified sugars. In some embodiments, the last three sugars are independently 2'-MOE modified sugars. In some embodiments, the last four sugars are independently 2'-MOE modified sugars. In some embodiments, each of such modified sugars is independently the sugar of a nucleoside whose nucleobase is optionally substituted or protected A, T, C, G, or U, or an optionally substituted or protected tautomer of A, T, C, G, or U. In some embodiments, one or more such sugars are independently bonded to a non-negatively charged internucleotidic linkage. In some embodiments, one or more such sugars are independently bonded to a neutral internucleotidic linkage such as n001. In some embodiments, a non-negatively charged internucleotidic linkage or neutral internucleotidic linkage, e.g., n001, is chirally controlled. In some embodiments, it is *R*p. In some embodiments, one or more such sugars are independently bonded to a phosphorothioate internucleotidic linkage. In some embodiments, a phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, it is *S*p. In some embodiments, as described herein, the internucleotidic linkage between the last and second last nucleosides is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n025. In some embodiments, In some embodiments, it is chirally controlled. In some embodiments, it is *R*p. In some embodiments, except the internucleotidic linkage between the last and second last nucleosides, each internucleotidic linkages bonded to nucleosides comprising the one or more of the last several, or the last several modified sugars are independently phosphorothioate internucleotidic linkages. In some embodiments, each is chirally controlled. In some

embodiments, each is *Sp*.

[00195] In some embodiments, a sugar at position +1 is a 2'-F modified sugar. In some embodiments, a sugar at position +1 is a natural DNA sugar. In some embodiments, a sugar at position 0 is a natural DNA sugar (nucleoside at position 0 is opposite to a target adenosine when aligned). In some embodiments, a sugar at position -1 is a DNA sugar. In some embodiments, a sugar at position -2 is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar (e.g., a sugar comprising 2'–O–CH_2–4', wherein the –CH_2– is optionally substituted (e.g., a LNA sugar, a cET sugar (e.g., (S)-cEt))). In some embodiments, it is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, it is a 2'-OMe modified sugar. In some embodiments, it is a 2'-MOE modified sugar. In some embodiments, it is a bicyclic sugar. In some embodiments, it is a LNA sugar. In some embodiments, it is a cEt sugar. In some embodiments, a sugar at position -3 is a 2'-F modified sugar. In some embodiments, each sugar after position -3 (e.g., position -4, -5, -6, etc.) is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar (e.g., a sugar comprising 2'–O–CH_2–4', wherein the –CH_2– is optionally substituted (e.g., a LNA sugar, a cET sugar (e.g., (S)-cEt))). In some embodiments, each is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each is a 2'-OMe modified sugar. In some embodiments, each is a 2'-MOE modified sugar. In some embodiments, one or more are independently 2'-OMe modified sugars, and one or more are independently 2'-MOE modified sugars. In some embodiments, as described herein, the internucleotidic linkage between nucleosides at positions -1 and-2 is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is chirally controlled. In some embodiments, it is *Sp*. In some embodiments, it is *Rp*. In some embodiments, the internucleotidic linkage between nucleosides at positions -2 and -3 is a natural phosphate linkage. In some embodiments, as described herein, the internucleotidic linkage between the last and second last nucleosides is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is chirally controlled. In some embodiments, it is *Rp*. In some embodiments, each internucleotidic linkages between nucleosides to the 3'-side of a nucleoside opposite to a target adenosine, except those between nucleosides at positions -1 and -2, and between nucleosides at positions -2 and -3, and between the last and the second last nucleosides, is independently a phosphorothioate internucleotidic linkages. In some embodiments, each phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, each is *Sp*.

[00196] In some embodiments, the first and/or last one or several sugars are modified sugars, e.g., bicyclic sugars and/or 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe modified sugars, 2'-MOE modified sugars, etc.). In some embodiments, such sugars may increase stability, affinity and/or activity of an oligonucleotide. In some embodiments, when conjugated to one or more additional

chemical moieties, sugars at 5'- and/or 3'-ends of oligonucleotides are not bicyclic sugars or 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 5'-end sugar is a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, such a 5'-end sugar is not connected to an additional chemical moiety. In some embodiments, a 5'-end sugar is a 2'-F modified sugar. In some embodiments, a 5'-end sugar is a 2'-F modified sugar conjugated to an additional chemical moiety. In some embodiments, a 3'-end sugar is a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, such a 3'-end sugar is not connected to an additional chemical moiety. In some embodiments, a 3'-end sugar is a 2'-F modified sugar. In some embodiments, a 3'-end sugar is a 2'-F modified sugar conjugated to an additional chemical moiety. In some embodiments, the last several sugars are 3'-side sugars relative to a nucleoside opposite to a target adenosine (e.g., sugars of 3'-side nucleosides such as N_{-1}, N_{-2}, etc.). In some embodiments, the last several sugars or the 3'-side sugars comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-F modified sugars. In some embodiments, the last several sugars or the 3'-side sugars comprises two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) consecutive 2'-F modified sugars. In some embodiments, the last several sugars or the 3'-side sugars comprises one or more, or two or more consecutive, 2'-F modified sugars, and sugar of the last nucleoside of an oligonucleotide is a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, as described herein a 2'-OR modified sugar is a 2'-OMe modified sugar or a 2'-MOE modified sugar; in some embodiments, it is a 2'-OMe modified sugar; in some embodiments, it is a 2'-MOE modified sugar. In some embodiments, the last several sugars or the 3'-side sugars comprises one or more, or two or more consecutive, 2'-F modified sugars, and sugar of the last nucleoside of an oligonucleotide is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the last several sugars or the 3'-side sugars comprises one or more, or two or more consecutive, 2'-F modified sugars, and sugar of the last nucleoside of an oligonucleotide is a 2'-OMe modified sugar or a 2'-MOE modified sugar. In some embodiments, the last several sugars or the 3'-side sugars comprises one or more, or two or more consecutive, 2'-F modified sugars, and sugar of the last nucleoside of an oligonucleotide is a 2'-OMe modified sugar. In some embodiments, the last several sugars or the 3'-side sugars comprises one or more, or two or more consecutive, 2'-F modified sugars, and sugar of the last nucleoside of an oligonucleotide is a 2'-MOE modified sugar. In some embodiments, two and no more than two nucleosides at the 3'-side of a nucleoside opposite to an adenosine independently have a 2'-F modified sugar. In some embodiments, they are at positions -4 and -5. In some embodiments, they are the second and third last nucleosides of an oligonucleotide. In some embodiments, one and no more than one nucleoside at the 3'-side of a nucleoside opposite to an adenosine has a 2'-F modified sugar. In some embodiments, it is at position -3. In some embodiments, it is 4th last nucleoside of an oligonucleotide.

[00197] In some embodiments, a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic is present in a region which comprises one or more (e.g., 1-30, 1-25, 1-20, 1-15, 1-10, 2-30, 2-25, 2-20, 2-25, 2-10, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more)

sugars are 2'-F modified. In some embodiments, a majority of sugars as described herein in such a region are 2'-F modified sugars. In some embodiments, two or more 2'-F modified sugars are consecutive. In some embodiments, a region is a first domain. In some embodiments, a bicyclic sugar is present in such a region. In some embodiments, a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic is present in such a region. In some embodiments, a 2'-OMe modified sugar is present in such a region. In some embodiments, a 2'-MOE modified sugar is present in such a region.

[00198] In some embodiments, one or more sugars at positions -5, -4, -3, +1, +2, +4, +5, +6, +7, and +8 (position 0 being the position of a nucleoside opposite to a target adenosine; "+" is going from a nucleoside opposite to a target adenosine toward 5'-end of an oligonucleotide, and "-" is going from a nucleoside opposite to a target adenosine toward 3'-end of an oligonucleotide; for example, in 5'-$N_1N_0N_{-1}$-3', if N_0 is a nucleoside opposite to a target adenosine, it is at position 0, and N_1 is at position +1 and N_{-1} is at position -1) are independently 2'-F modified sugars. In some embodiments, a sugar at position +1, and one or more sugars at positions -5, -4, -3, +2, +4, +5, +6, +7, and +8, are independently 2'-F modified sugars. In some embodiments, a sugar at position +1, and one sugar at position -5, -4, -3, +2, +4, +5, +6, +7, and +8, are independently 2'-F modified sugars.

[00199] In some embodiments, an oligonucleotide comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more, 2-10, 3-10, 2-5, 2-4, 2-3, 3-5, 3-4, etc.) natural DNA sugars. In some embodiments, one or more natural DNA sugars are at an editing region, e.g., positions +1, 0, and/or -1. In some embodiments, a natural DNA sugar is within the first several nucleosides of an oligonucleotides (e.g., the first 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleosides). In some embodiments, the first, second, and/or third nucleosides of an oligonucleotides independently have a natural DNA sugar. In some embodiments, a natural DNA sugar is bonded to a modified internucleotidic linkage such as a non-negatively charged internucleotidic linkage, a neutral internucleotidic linkage, a phosphoryl guanidine internucleotidic linkage, n001, or a phosphorothioate internucleotidic linkage (in various embodiments, *Sp*).

[00200] Oligonucleotides may contain various types of internucleotidic linkages. In some embodiments, oligonucleotides comprises one or more modified internucleotidic linkages. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkages. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is n001. In some embodiments, oligonucleotides comprises one or more natural phosphate linkages. In some embodiments, a natural phosphate linkage bonds to a nucleoside comprising a modified sugar that can improve stability (e.g., resistance toward nuclease). In some embodiments, a natural phosphate linkage bonds to a bicyclic sugar. In some embodiments, a natural phosphate linkage bonds to a 2'-modified sugar. In some embodiments, a natural phosphate linkage bonds to a 2'-OR modified sugar, wherein

R is optionally substituted C_{1-6} aliphatic. In some embodiments, a natural phosphate linkage bonds to a 2'-OMe modified sugar. In some embodiments, a natural phosphate linkage bonds to a 2'-MOE modified sugar. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage, a non-negatively charged internucleotidic linkage, and a natural phosphate linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage, a neutral internucleotidic linkage, and a natural phosphate linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage, a phosphoryl guanidine internucleotidic linkage, and a natural phosphate linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage, n001, and a natural phosphate linkage. In some embodiments, each chiral internucleotidic linkage is independently chirally controlled. In some embodiments, one or more chiral internucleotidic linkage is not chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, each chiral internucleotidic linkage is independently chirally controlled. In some embodiments, a majority or each phosphorothioate internucleotidic linkage is *Sp* as described herein. In some embodiments, a majority or each non-negatively charged internucleotidic linkage, e.g., n001, is *Rp*. In some embodiments, a majority or each non-negatively charged internucleotidic linkage, e.g., n001, is *Sp*.

[00201] In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage and a non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage and a neutral internucleotidic linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage and a phosphoryl guanidine internucleotidic linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage and n001. In some embodiments, each chiral internucleotidic linkage is independently chirally controlled. In some embodiments, one or more chiral internucleotidic linkage is not chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, each chiral internucleotidic linkage is independently chirally controlled. In some embodiments, a majority or each phosphorothioate internucleotidic linkage is *Sp* as described herein. In some embodiments, one or more (e.g., 1, 2, 3, 4, or 5) phosphorothioate internucleotidic linkages are *Rp*. In some embodiments, a majority or each non-negatively charged internucleotidic linkage, e.g., n001, is *Rp*. In some embodiments, a majority or each non-negatively charged internucleotidic linkage, e.g., n001, is *Sp*. In some embodiments, an oligonucleotide comprises no natural phosphate linkages. In some embodiments, each internucleotidic linkage is independently a phosphorothioate or a non-negatively charged internucleotidic linkage. In some embodiments, each internucleotidic linkage is independently a phosphorothioate or a neutral charged internucleotidic linkage. In some embodiments, each internucleotidic linkage is independently a phosphorothioate or phosphoryl guanidine internucleotidic linkages. In some embodiments, each internucleotidic linkage is independently a phosphorothioate or n001 internucleotidic linkage. In some embodiments, the last internucleotidic linkage of an oligonucleotide is a non-negatively charged internucleotidic linkage, or is a neutral internucleotidic linkage, or is a phosphoryl guanidine internucleotidic

linkage, or is n001.

[00202] In some embodiments, oligonucleotides of the present disclosure comprise one or more modified nucleobases. Various modifications can be introduced to a sugar and/or nucleobase in accordance with the present disclosure. For example, in some embodiments, a modification is a modification described in US 9006198. In some embodiments, a modification is a modification described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the sugars, bases, and internucleotidic linkages of each of which are independently incorporated herein by reference.

[00203] In some embodiments, a nucleobase in a nucleoside is or comprises Ring BA which has the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA, wherein the nucleobase is optionally substituted or protected.

[00204] In some embodiments, a sugar is a modified sugar comprising a 2'-modificatin, e.g., 2'-F, 2'-OR wherein R is optionally substituted aliphatic, or a bicyclic sugar (e.g., a LNA sugar), or a acyclic sugar (e.g., a UNA sugar).

[00205] In some embodiments, as described herein, provided oligonucleotides comprise one or more domains, each of which independently has certain lengths, modifications, linkage phosphorus stereochemistry, etc., as described herein. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars and/or one or more modified internucleotidic linkages, wherein the oligonucleotide comprises a first domain and a second domain each independently comprising one or more nucleobases. In some embodiments, the present disclosure provides oligonucleotide comprising one or more domains and/or subdomains as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising a first domain as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising a second domain as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising a first subdomain as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising a second subdomain as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising a third subdomain as described herein. In some embodiments, the present disclosure provides oligonucleotides comprising one or more regions each independently selected from a first domain, a second domain, a first subdomain, a second subdomain and a third subdomain, each of which is independently as described herein. In some embodiments, the present disclosure provides an oligonucleotide comprising:

a first domain; and

a second domain,

wherein:

the first domain comprises one or more 2'-F modifications;

the second domain comprises one or more sugars that do not have a 2'-F modification.

[00206] In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar). In some embodiments, a modified sugar comprises a 5'-modification. Typically, oligonucleotides of the present disclosure have a free 5'-OH at its 5'-end and a free 3'-OH at its 3'-end unless indicated otherwise, e.g., by context. In some embodiments, a 5'-end sugar of an oligonucleotide may comprise a modified 5'-OH.

[00207] In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all sugars in an oligonucleotide or a portion thereof, respectively. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%.

[00208] In some embodiments, a majority is at least 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more. In some embodiments, a majority is about 50%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%. In some embodiments, a majority is about or at least about 50%. In some embodiments, a majority is about or at least about 55%. In some embodiments, a majority is about or at least about 60%. In some embodiments, a majority is about or at least about 65%. In some embodiments, a majority is about or at least about 70%. In some embodiments, a majority is about or at least about 75%. In some embodiments, a majority is about or at least about 80%. In some embodiments, a majority is about or at least about 85%. In some embodiments, a majority is about or at least about 90%. In some embodiments, a majority is about or at least about 95%.

[00209] In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of modified internucleotidic linkages. In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of chiral internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%.

[00210] In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of chirally controlled internucleotidic linkages. In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of *Sp* internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a

percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%.

[00211] In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of *Sp* internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, about 1-50, 1-40, 1-30, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *Sp* chiral internucleotidic linkages. In many embodiments, it was observed that a high percentage (e.g., relative to *Rp* internucleotidic linkages and/or natural phosphate linkages) of *Sp* internucleotidic linkages in an oligonucleotide or certain portions thereof can provide improved properties and/or activities, e.g., high stability and/or high adenosine editing activity.

[00212] In some embodiments, an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.) comprises a certain level of *R*p internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in an oligonucleotide or a portion thereof, respectively. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, about 1-50, 1-40, 1-30, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *R*p chiral internucleotidic linkages. In some embodiments, the number is about or no more than

about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the number is about or no more than about 3. In some embodiments, the number is about or no more than about 4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10.

[00213] In some embodiments, an oligonucleotide comprises one or more features selected from: (i) the first 3 sugars from the 5'-end of the oligonucleotide independently comprise 2'-MOE; (ii) the first internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage; (iii) a mismatch or wobble base-pairing at position N_{20}; (iv) a 2'-OMe modified sugar at position N_{19}; (v) a 2'-MOE modified sugar at position N_{17}; (v) a PN linkage between positions N_{13} and N_{12}; (vi) a PN linkage between positions N_{12} and N_{11}; (vii) at least one 2'-OMe modified sugar at a position selected from N_{13}, N_{12}, and N_{11}; (viii) a nucleobase at position N_9 that produces a G-U wobble base pairing when aligned with a target nucleic acid; (ix) a PN linkage between positions N_9 and N_8; (x) a 2'-OMe modified sugar at position N_8; (xi) a natural DNA sugar at position N_1; (xii) n3U nucleobase at position N_0; (xiii) a PN linkage between positions N_{-1} and N_{-2}; (xiv) a natural DNA sugar at position N_{-1}; (xv) a 2'-OMe at position N_{-2}; (xvi) a 2'-F at position N_{-3}; (xvii) the first 2 sugars from the 3'-end of the oligonucleotide independently comprise 2'-OMe; and (xviii) the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN linkage. In some embodiments, an oligonucleotide comprises all these features. In some embodiments, each of the other sugars is independently a 2'-F modified sugar. In some embodiments, each of the other internucleotidic linkages is independently a phosphorothioate linkage. In some embodiments, each of the other internucleotidic linkages is independently a *Sp* phosphorothioate linkage.

[00214] In some embodiments, an oligonucleotide comprises one or more features selected from: (i) the first 3 sugars from the 5'-end of the oligonucleotide independently comprise 2'-MOE; (ii) the first internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage; (iii) a mismatch or wobble base-pairing at the 5th nucleoside from the 5'-end of the oligonucleotide; (iv) a 2'-OMe modified sugar at the 6th nucleoside from the 5'-end of the oligonucleotide; (v) a 2'-MOE modified sugar at the 8th nucleoside from the 5'-end of the oligonucleotide; (v) a PN linkage between the 12th nucleoside from the 5'-end of the oligonucleotide and the 13th nucleoside from the 5'-end of the oligonucleotide; (vi) a PN linkage between the 13th nucleoside from the 5'-end of the oligonucleotide and the 14th nucleoside from the 5'-end of the oligonucleotide; (vii) at least one 2'-OMe modified sugar at a position selected from the 12th nucleoside from the 5'-end of the oligonucleotide, the 13th nucleoside from the 5'-end of the oligonucleotide, and the 14th nucleoside from the 5'-end of the oligonucleotide; (viii) a nucleobase at the 16th nucleoside from the 5'-end of the oligonucleotide that produces a G-U wobble base pairing when aligned with a target nucleic acid; (ix) a PN linkage between the 16th nucleoside from the 5'-end of the oligonucleotide and the 17th nucleoside from the 5'-end of the oligonucleotide; (x) a 2'-OMe modified sugar at the 17th nucleoside from the 5'-end of the

oligonucleotide; (xi) a natural DNA sugar at the 24th nucleoside from the 5'-end of the oligonucleotide; (xii) n3U nucleobase at the 25th nucleoside from the 5'-end of the oligonucleotide; (xiii) a PN linkage between the 5th nucleoside from the 3'-end of the oligonucleotide and the 4th nucleoside from the 3'-end of the oligonucleotide; (xiv) a natural DNA sugar at the 5th nucleoside from the 3'-end of the oligonucleotide; (xv) a 2'-OMe at the 4th nucleoside from the 3'-end of the oligonucleotide; (xvi) a 2'-F at the 3th nucleoside from the 3'-end of the oligonucleotide; (xvii) the first 2 sugars from the 3'-end of the oligonucleotide independently comprise 2'-OMe; and (xviii) the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN linkage. In some embodiments, an oligonucleotide comprises all these features. In some embodiments, each of the other sugars is independently a 2'-F modified sugar. In some embodiments, each of the other internucleotidic linkages is independently a phosphorothioate linkage. In some embodiments, each of the other internucleotidic linkages is independently a *Sp* phosphorothioate linkage.

[00215] In some embodiments, an oligonucleotide comprises one or more features selected from: (i) the first 3 sugars from the 5'-end of the oligonucleotide independently comprise 2'-MOE; (ii) the first internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage; (iii) a mismatch or wobble base-pairing at the 5th nucleoside from the 5'-end of the oligonucleotide; (iv) a 2'-OMe modified sugar at the 6th nucleoside from the 5'-end of the oligonucleotide; (v) a 2'-MOE modified sugar at the 8th nucleoside from the 5'-end of the oligonucleotide; (v) a PN linkage between the 12th nucleoside from the 5'-end of the oligonucleotide and the 13th nucleoside from the 5'-end of the oligonucleotide; (vi) a PN linkage between the 13th nucleoside from the 5'-end of the oligonucleotide and the 14th nucleoside from the 5'-end of the oligonucleotide; (vii) at least one 2'-OMe modified sugar at a position selected from the 12th nucleoside from the 5'-end of the oligonucleotide, the 13th nucleoside from the 5'-end of the oligonucleotide, and the 14th nucleoside from the 5'-end of the oligonucleotide; (viii) a nucleobase at the 16th nucleoside from the 5'-end of the oligonucleotide that produces a G-U wobble base pairing when aligned with a target nucleic acid; (ix) a PN linkage between the 16th nucleoside from the 5'-end of the oligonucleotide and the 17th nucleoside from the 5'-end of the oligonucleotide; (x) a 2'-OMe modified sugar at the 17th nucleoside from the 5'-end of the oligonucleotide; (xi) a natural DNA sugar at the 24th nucleoside from the 5'-end of the oligonucleotide; (xii) n3U nucleobase at the 6th nucleoside from the 3'-end of the oligonucleotide; (xiii) a PN linkage between the 5th nucleoside from the 3'-end of the oligonucleotide and the 4th nucleoside from the 3'-end of the oligonucleotide; (xiv) a natural DNA sugar at the 5th nucleoside from the 3'-end of the oligonucleotide; (xv) a 2'-OMe at the 4th nucleoside from the 3'-end of the oligonucleotide; (xvi) a 2'-F at the 3th nucleoside from the 3'-end of the oligonucleotide; (xvii) the first 2 sugars from the 3'-end of the oligonucleotide independently comprise 2'-OMe; and (xviii) the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN linkage. In some embodiments, an oligonucleotide comprises all these features. In some embodiments, each of the other sugars is independently a 2'-F modified sugar. In some embodiments, each of the other internucleotidic linkages is independently a phosphorothioate linkage. In some embodiments, each of the other internucleotidic linkages is independently a *Sp* phosphorothioate linkage.

[00216] While not wishing to be bound by theory, it is noted that in some instances *R*p and *S*p configurations of internucleotidic linkages may affect structural changes in helical conformations of double stranded complexes formed by oligonucleotides and target nucleic acids such as RNA, and ADAR proteins may recognize and interact various targets (e.g., double stranded complexes formed by oligonucleotides and target nucleic acids such as RNA) through multiple domains. In some embodiments, provided oligonucleotides and compositions thereof promote and/or enhance interaction profiles of oligonucleotide, target nucleic acids, and/or ADAR proteins to provide efficient adenosine modification by ADAR proteins through incorporation of various modifications and/or control of stereochemistry.

[00217] In some embodiments, an oligonucleotide can have or comprise a base sequence; internucleotidic linkage, base modification, sugar modification, additional chemical moiety, or pattern thereof; and/or any other structural element described herein, e.g., in a Table.

[00218] In some embodiments, a provided oligonucleotide or composition is characterized in that, when it is contacted with a target nucleic acid comprising a target adenosine in a system (e.g., an ADAR-mediated deamination system), modification of the target adenosine (e.g., deamination of the target A) is improved relative to that observed under reference conditions (e.g., selected from the group consisting of absence of the composition, presence of a reference oligonucleotide or composition, and combinations thereof). In some embodiments, modification, e.g., ADAR-mediated deamination (e.g., endogenous ADAR-mediated deamination) is increased 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000 fold or more.

[00219] In some embodiments, oligonucleotides are provided as salt forms. In some embodiments, oligonucleotides are provided as salts comprising negatively-charged internucleotidic linkages (e.g., phosphorothioate internucleotidic linkages, natural phosphate linkages, etc.) existing as their salt forms. In some embodiments, oligonucleotides are provided as pharmaceutically acceptable salts. In some embodiments, oligonucleotides are provided as metal salts. In some embodiments, oligonucleotides are provided as sodium salts. In some embodiments, oligonucleotides are provided as ammonium salts. In some embodiments, oligonucleotides are provided as metal salts, e.g., sodium salts, wherein each negatively-charged internucleotidic linkage is independently in a salt form (e.g., for sodium salts, −O−P(O)(SNa)−O− for a phosphorothioate internucleotidic linkage, −O−P(O)(ONa)−O− for a natural phosphate linkage, etc.).

[00220] In some embodiments, oligonucleotides are chiral controlled, comprising one or more chirally controlled internucleotidic linkages. In some embodiments, provided oligonucleotides are stereochemically pure. In some embodiments, provided oligonucleotides or compositions thereof are substantially pure of other stereoisomers. In some embodiments, the present disclosure provides chirally controlled oligonucleotide compositions.

[00221] As described herein, oligonucleotides of the present disclosure can be provided in high purity (e.g., 50%-100%). In some embodiments, oligonucleotides of the present disclosure are of high stereochemical

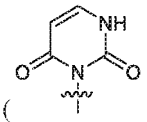
purity (e.g., 50%-100%). In some embodiments, oligonucleotides in provided compositions are of high stereochemical purity (e.g., high percentage (e.g., 50%-100%) of a stereoisomer compared to the other stereoisomers of the same oligonucleotide). In some embodiments, a percentage is at least or about 50%. In some embodiments, a percentage is at least or about 60%. In some embodiments, a percentage is at least or about 70%. In some embodiments, a percentage is at least or about 75%. In some embodiments, a percentage is at least or about 80%. In some embodiments, a percentage is at least or about 85%. In some embodiments, a percentage is at least or about 90%. In some embodiments, a percentage is at least or about 95%.

[00222] In some embodiments, oligonucleotides of the present disclosure are at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% stereochemically pure at linkage phosphorus of chiral internucleotidic linkages. In some embodiments, oligonucleotides of the present disclosure are prepared stereoselectively and are substantially free of stereoisomers. In some embodiments, in provided compositions comprising a plurality of oligonucleotides which share the same base sequence of the same pattern of chiral linkage phosphorus stereochemistry (e.g., comprising one or more of *Rp* and/or *Sp*, wherein each chiral linkage phosphorus is independently *Rp* or *Sp*), at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% of all oligonucleotides in the composition that share the same base sequence as oligonucleotides of the plurality share the same pattern of chiral linkage phosphorus stereochemistry or are oligonucleotides of the plurality. In some embodiments, in provided compositions comprising a plurality of oligonucleotides which share the same base sequence of the same pattern of chiral linkage phosphorus stereochemistry, at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% of all oligonucleotides in the composition that share the same constitution as oligonucleotides of the plurality share the same pattern of chiral linkage phosphorus stereochemistry or are oligonucleotides of the plurality. In some embodiments, diastereomeric purity of a chiral phosphorus is about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, diastereomeric purity of each phosphorothioate internucleotidic linkage is independently about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, diastereomeric purity of each linkage phosphorus is independently about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, diastereomeric purity of each chiral phosphorus is about or at least about 90%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 95%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 97%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 98%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 90%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 95%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 97%. In some embodiments, diastereomeric excess of each chiral phosphorus is independently about or at least about 98%. In some embodiments, diastereomeric purity is about or at least about $(DS)^{nc}$, wherein DS is about 90-100%, and nc is the number of chiral linkage phosphorus. In some embodiments, DS is about 90% or more. In some embodiments, DS is

about 95% or more. In some embodiments, DS is about 96% or more. In some embodiments, DS is about 97% or more. In some embodiments, DS is about 98% or more. In some embodiments, DS is about 99% or more. In some embodiments, diastereomeric purity is represented as the product of the diastereopurity of each chiral linkage phosphorus.

[00223] In some embodiments, the internucleotidic linkage between N_{23} and N_{22} is a natural phosphate linkage. In some embodiments, the 2nd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_{22} and N_{21} is a natural phosphate linkage. In some embodiments, the 3rd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_{17} and N_{16} is a natural phosphate linkage. In some embodiments, the 8th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_{11} and N_{10} is a natural phosphate linkage. In some embodiments, the 14th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage or a PS internucleotidic linkage. In some embodiments, the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage or a PS internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage. In some embodiments, the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_6 and N_5 is a natural phosphate linkage or a PS internucleotidic linkage. In some embodiments, the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage or a PS internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_6 and N_5 is a natural phosphate linkage. In some embodiments, the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage. In some embodiments, the 27th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage. In some embodiments, the internucleotidic linkage between N_{24} and N_{23} is a PN linkage. In some embodiments, the 1st internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage. In some embodiments, the internucleotidic linkage between N_{13} and N_{12} is a PN or a PS linkage. In some embodiments, the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or PS linkage. In some embodiments, the internucleotidic linkage between N_{13} and N_{12} is a PS linkage. In some embodiments, the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage. In some embodiments, the internucleotidic linkage between N_{12} and N_{11} is a PN linkage. In some embodiments, the 13th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage. In some embodiments, the internucleotidic linkage between N_9 and N_8 is a PN or a PS linkage. In some embodiments, the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or PS linkage. In some embodiments, the internucleotidic linkage between N_9 and N_8 is a PN linkage. In some embodiments, the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage. In some embodiments,

the internucleotidic linkage between N_{-1} and N_{-2} is a PN or a methylphosphonate linkage. In some embodiments, it is a PN linkage. In some embodiments, it is a methylphosphonate linkage. In some embodiments, the 26th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or a methylphosphonate linkage. In some embodiments, it is a PN linkage. In some embodiments, it is a methylphosphonate linkage. In some embodiments, the internucleotidic linkage between N_{-1} and N_{-2} is a PN linkage. In some embodiments, the 26th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage. In some embodiments, the internucleotidic linkage between N_{-4} and N_{-5} is a PN linkage. In some embodiments, the 29th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage. In some embodiments, the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_1 and N_0 is a PS linkage. In some embodiments, the 24th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage. In some embodiments, the internucleotidic linkage between N_0 and N_{-1} is a PS linkage. In some embodiments, the 25th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage. In some embodiments, the internucleotidic linkage between N_{-3} and N_{-4} is a PS linkage. In some embodiments, the 28th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage. In some embodiments, the first internucleotidic linkage of the 5'-end of oligonucleotide is a PN internucleotidic linkage. In some embodiments, the first internucleotidic linkage of the 3'-end of oligonucleotide is a PN internucleotidic linkage. In some embodiments, the PN internucleotidic linkage is a phosphoramidate internucleotidic linkage. In some embodiments, the PN internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a PN internucleotidic linkage is n001. In some embodiments, a PN internucleotidic linkage is n006. In some embodiments, a PN internucleotidic linkage is MsPA. In some embodiments, a linkage phosphorus of the PN internucleotidic linkage is *R*p. In some embodiments, each internucleotidic linkage is independently a natural phosphate linkage, a PS internucleotidic linkage, or a PN internucleotidic linkage. In some embodiments, each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each phosphorothioate internucleotidic linkage is independently *S*p. In some embodiments, each PN internucleotidic linkage is independently a phosphoramidate internucleotidic linkage.

The oligonucleotide of any one of the preceding claims, wherein the nucleobase of N_0 is [3nU] (). In some embodiments, sugar of N_0 is a 2'-OMe modified sugar. In some embodiments, sugar of N_1 is a natural DNA sugar, or a 2'-modified sugar. In some embodiments, sugar of N_{-1} is a natural DNA sugar. In some embodiments, sugar of N_{-2} is a 2'-OMe modified sugar. In some embodiments, sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, sugar of each of N_{24}, N_{23}, and/or N_{22} is independently a 2'-OR modified sugar. In some embodiments, each of the 1st, 2nd and/or 3rd sugars from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar. In some embodiments, sugar of N_{27} is a 2'-OR modified sugar. In

some embodiments, the 8th sugar from the 5'-end of the oligonucleotide is a 2'-OR modified sugar. In some embodiments, a 2'-OR modified sugar is a 2'-MOE modified sugar. In some embodiments, sugar of each of N_{29}, N_{11}, and/or N_8 is independently a 2'-OR modified sugar. In some embodiments, each of the 6th, 14th and 17th sugars from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar. In some embodiments, sugar of each of N_{-4}, and/or N_{-5} is independently a 2'-OR modified sugar. In some embodiments, each of the last sugar and the second last sugar from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar. In some embodiments, a 2'-OR modified sugar is a 2'-OMe modified sugar. In some embodiments, sugar of each of N_{21}, N_{18}, N_{16}, N_{15}, N_{14}, N_{10}, N_9, N_7, N_5, N_4, N_3 and/or N_2 is independently a 2'-F modified sugar. In some embodiments, each of them is a 2'-F modified sugar. In some embodiments, each of the 4th, 7th, 9th, 10th, 11th, 15th, 16th, 18th, 20th, 21st, 22nd and/or 23rd sugars from the 5'-end of the oligonucleotide is independently a 2'-F modified sugar. In some embodiments, each of them is a 2'-F modified sugar.

[00224] In some embodiments, an oligonucleotide is an oligonucleotide selected from:

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[

Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0; and

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0,

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ss

p].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

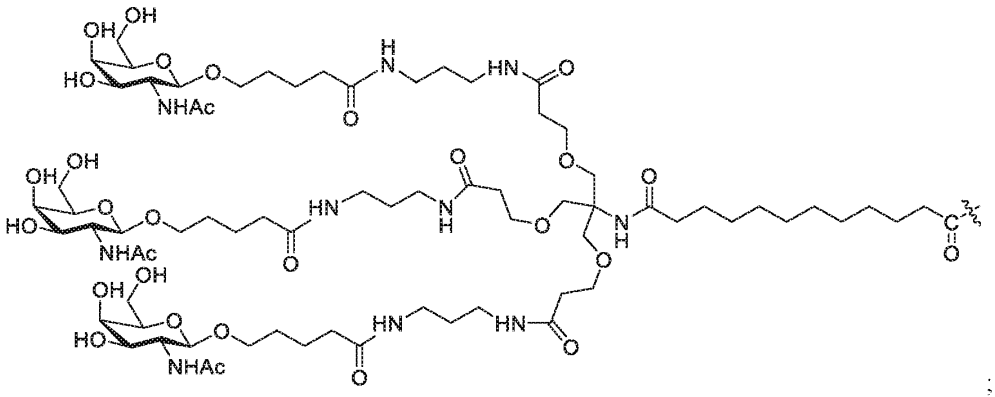
RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

or a salt thereof, wherein:

[GalNAc3C12oyl] represents



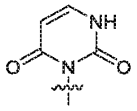
;

[nC6o] represents $-NH(CH_2)_6-$, wherein –NH– is bonded to [GalNAc3C12oyl], and the end $-CH_2-$ is bonded to an oxygen atom that is bonded to the linkage phosphorus of a phosphate linkage;

d represents a natural DNA sugar in a nucleoside;

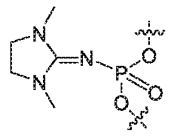
m represents a 2'-OMe modified sugar in a nucleoside;

[fl2r] represents a 2'-F modified sugar in a nucleoside;

[3nU] represents a nucleoside whose base is ;

p represents a phosphate linkage;

[Ssp] represents a phosphorothioate linkage in the *Sp* configuration; and



[n001R] represents wherein the phosphorus is of the *R*p configuration.

In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](

G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In

some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof. In some embodiments, an oligonucleotide is or comprises RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0, or a salt thereof.

[00225] In some embodiments, the present disclosure provides a compound having the structure of formula A-1 (Compound A-1) or a salt thereof. In some embodiments, an oligonucleotide is Compound A-1 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound A-1 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound A-1 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111146 comprises Compound A-1 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

[00226] In some embodiments, the present disclosure provides a compound having the structure of formula A-2 (Compound A-2) or a salt thereof. In some embodiments, an oligonucleotide is Compound A-2 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound A-2 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound A-2 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111148 comprises Compound A-2 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

[00227] In some embodiments, the present disclosure provides a compound having the structure of formula A-3 (Compound A-3) or a salt thereof. In some embodiments, an oligonucleotide is Compound A-3 or a salt

thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound A-3 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound A-3 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111820 comprises Compound A-3 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

[00228] In some embodiments, the present disclosure provides a compound having the structure of formula A-4 (Compound A-4) or a salt thereof. In some embodiments, an oligonucleotide is Compound A-4 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound A-4 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound A-4 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111776 comprises Compound A-4 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

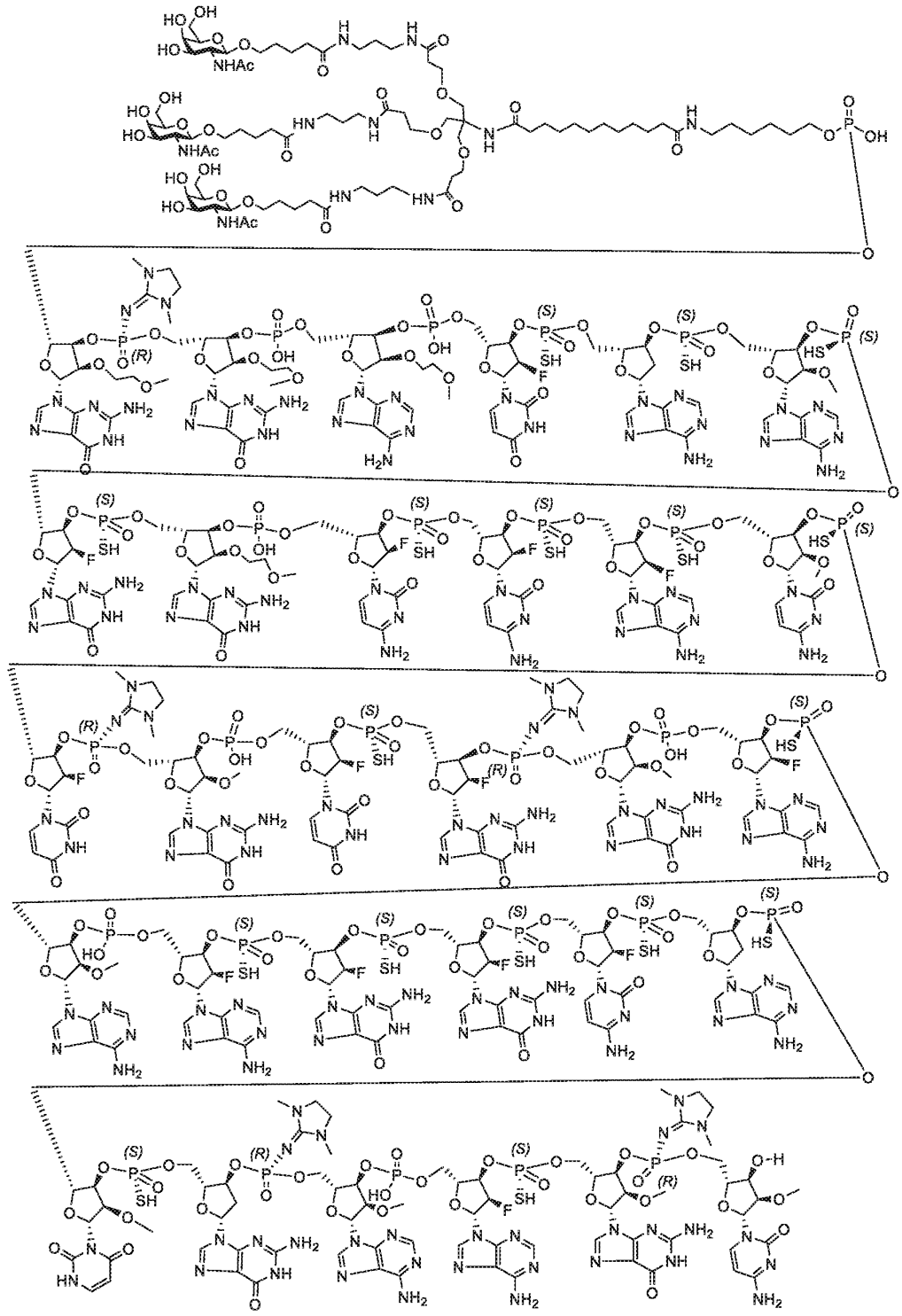
[00229] In some embodiments, the present disclosure provides a compound having the structure of formula B-1 (Compound B-1) or a salt thereof. In some embodiments, an oligonucleotide is Compound B-1 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound B-1 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound B-1 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111146-B comprises Compound B-1 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

[00230] In some embodiments, the present disclosure provides a compound having the structure of formula B-2 (Compound B-2) or a salt thereof. In some embodiments, an oligonucleotide is Compound B-2 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound B-2 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound B-2 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111148-B comprises Compound B-2 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

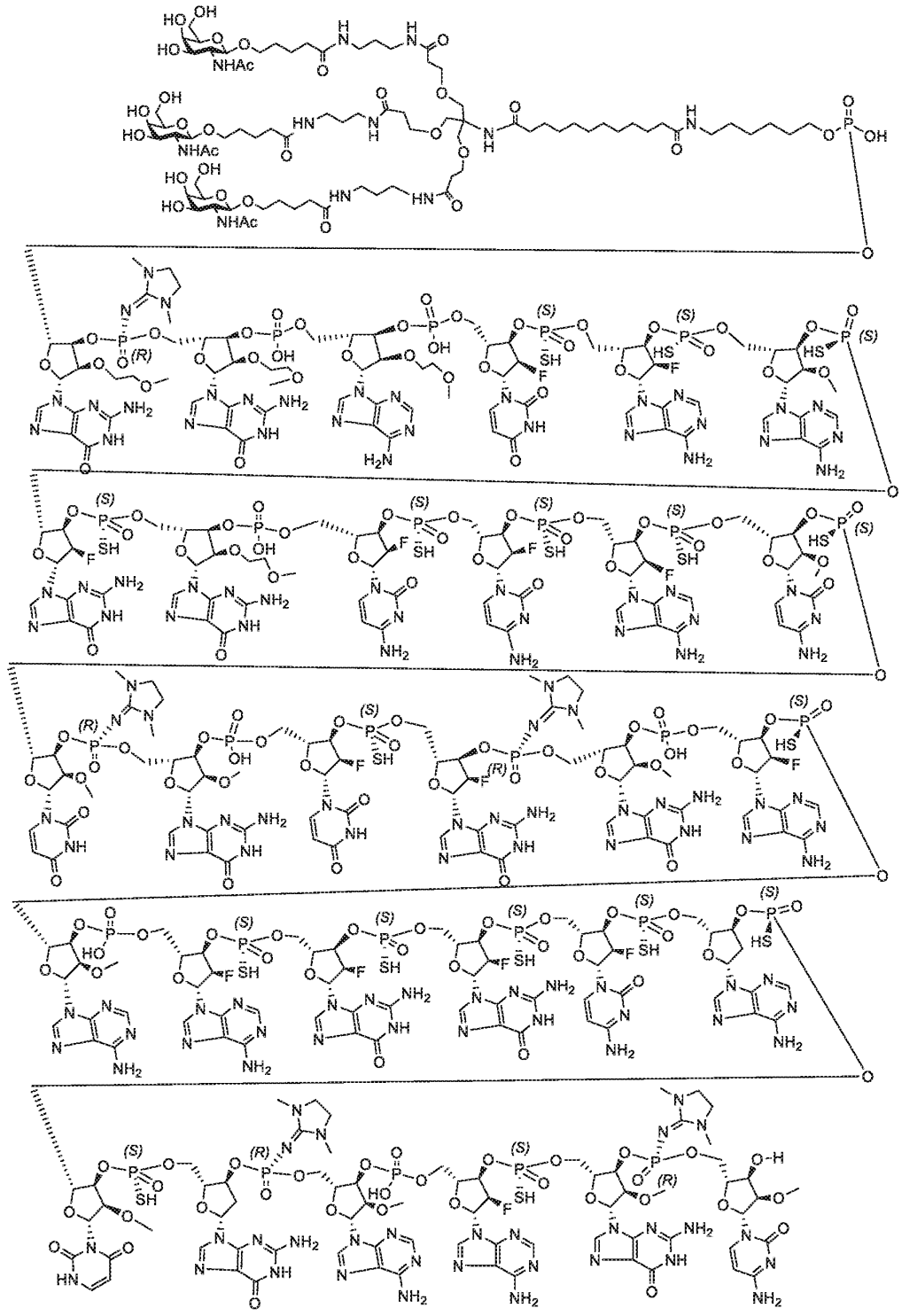
[00231] In some embodiments, the present disclosure provides a compound having the structure of formula B-3 (Compound B-3) or a salt thereof. In some embodiments, an oligonucleotide is Compound B-3 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound B-3 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound B-3 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111820-B comprises Compound B-3 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.

[00232] In some embodiments, the present disclosure provides a compound having the structure of formula B-4 (Compound B-4) or a salt thereof. In some embodiments, an oligonucleotide is Compound B-4 or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) comprises Compound B-4

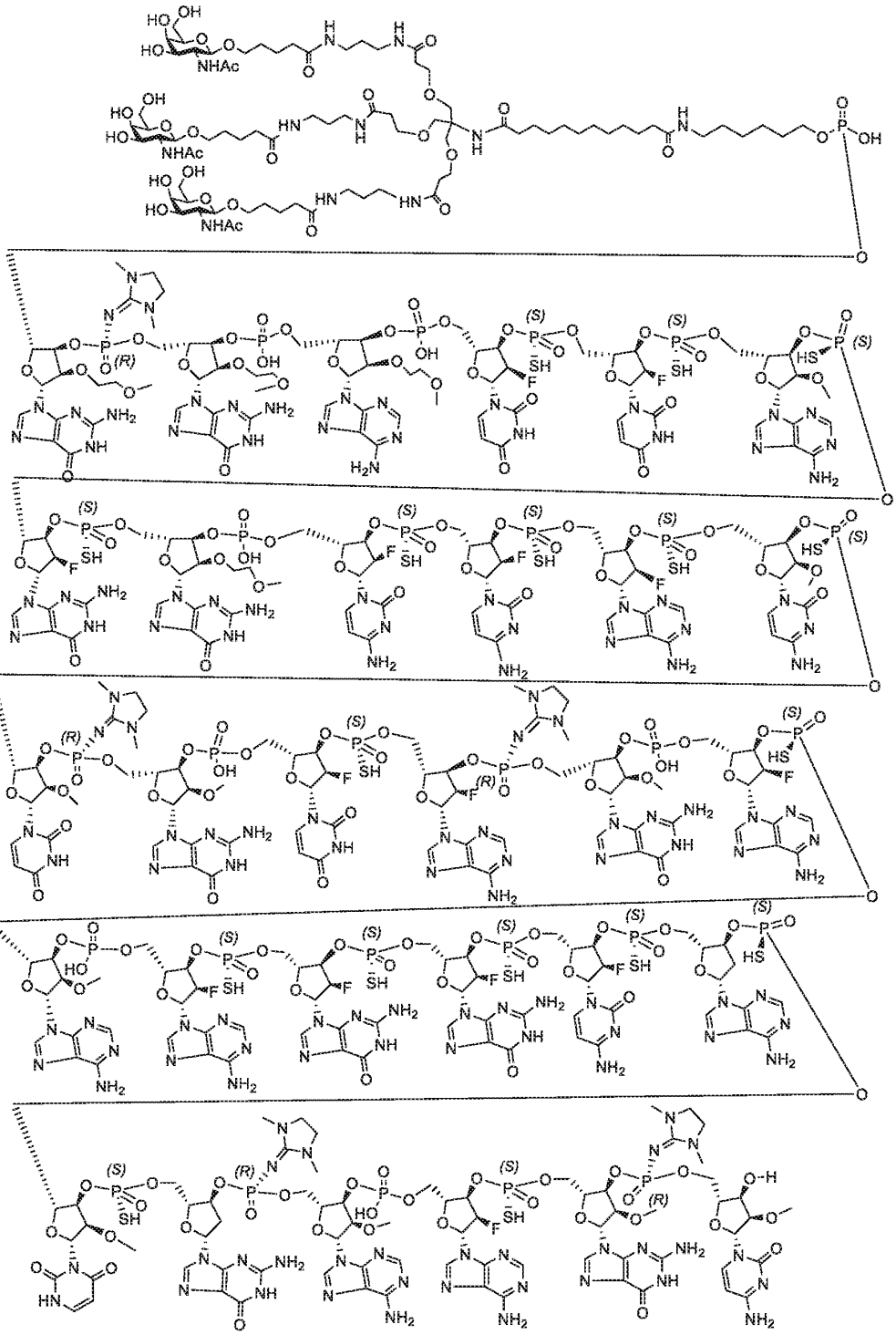
or a salt thereof. In some embodiments, a composition (e.g., a pharmaceutical composition) delivers Compound B-4 or a salt thereof. In some embodiments, a composition (e.g., a preparation) of ADR-0111776-B comprises Compound B-4 or a salt thereof. In some embodiments, a composition is a pharmaceutical composition. In some embodiments, a composition is chirally controlled.



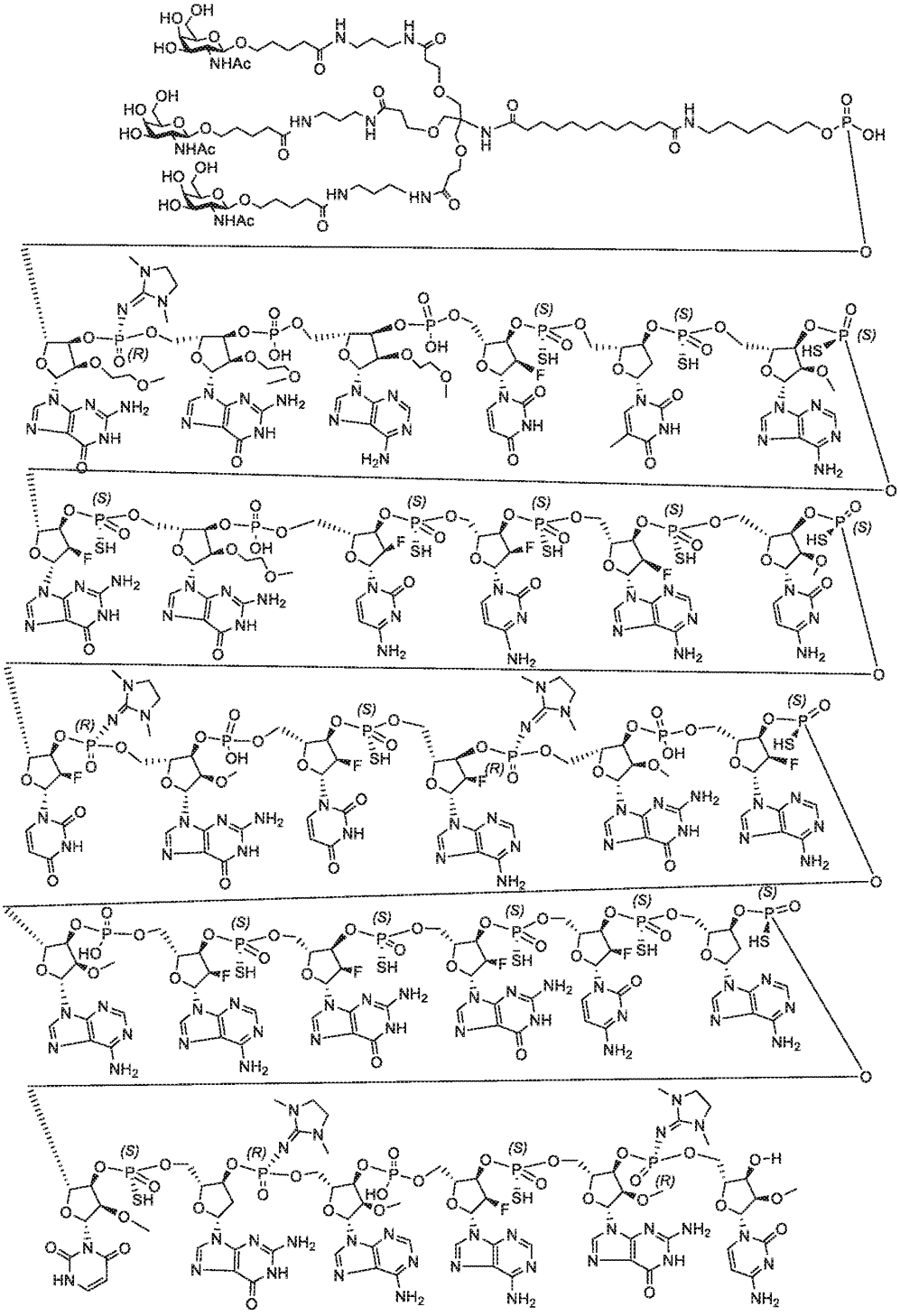
A-1



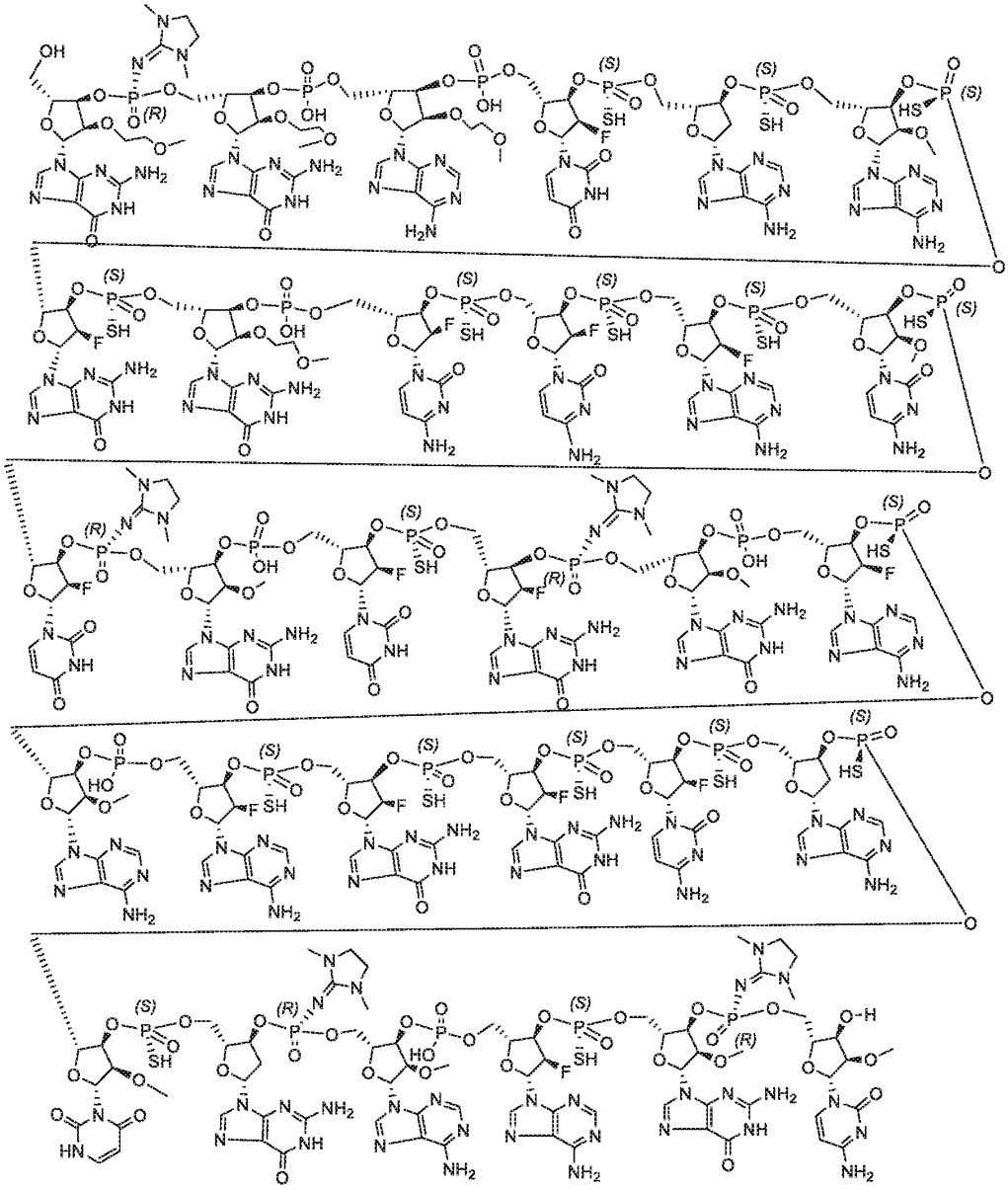
A-2



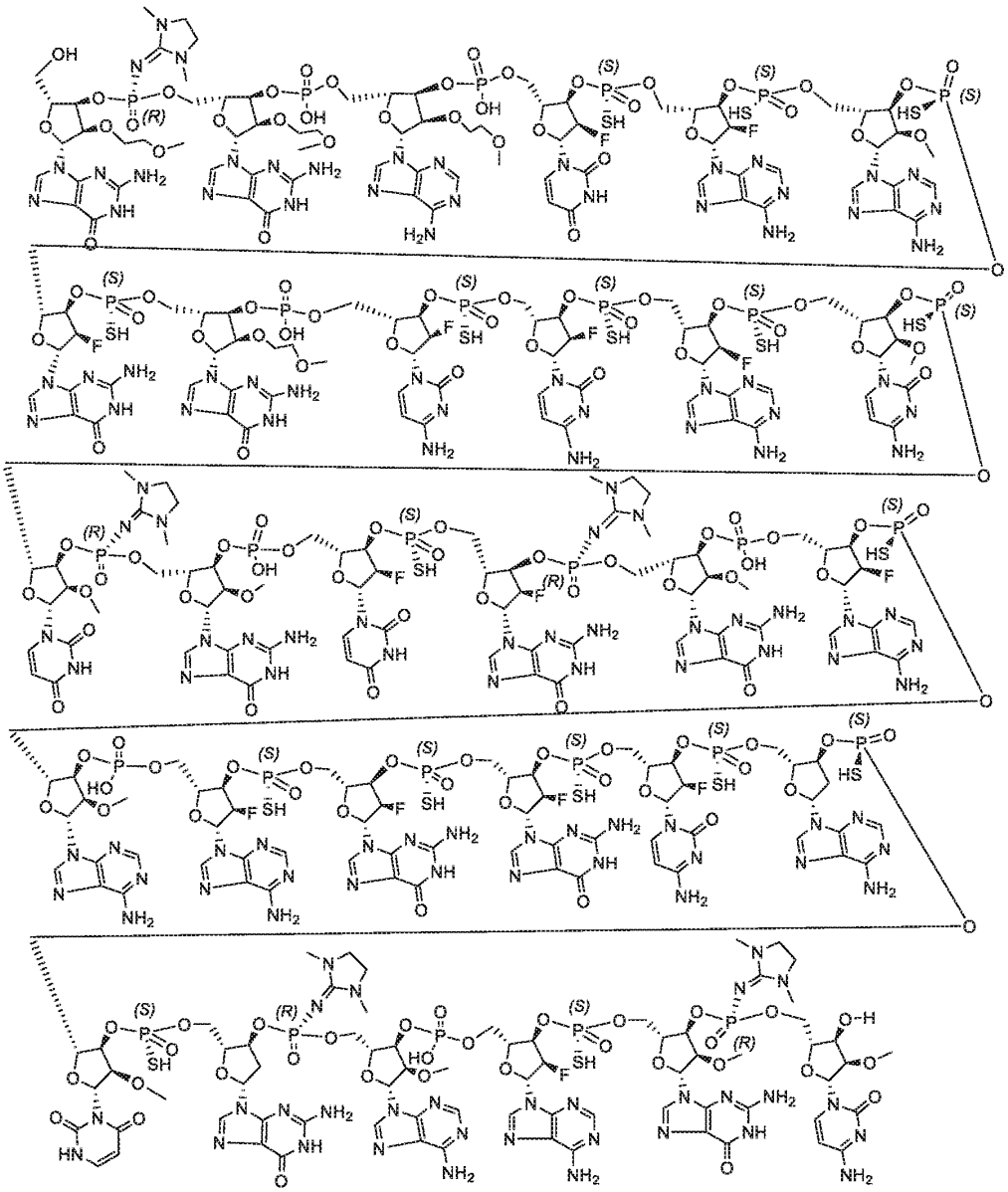
A-3



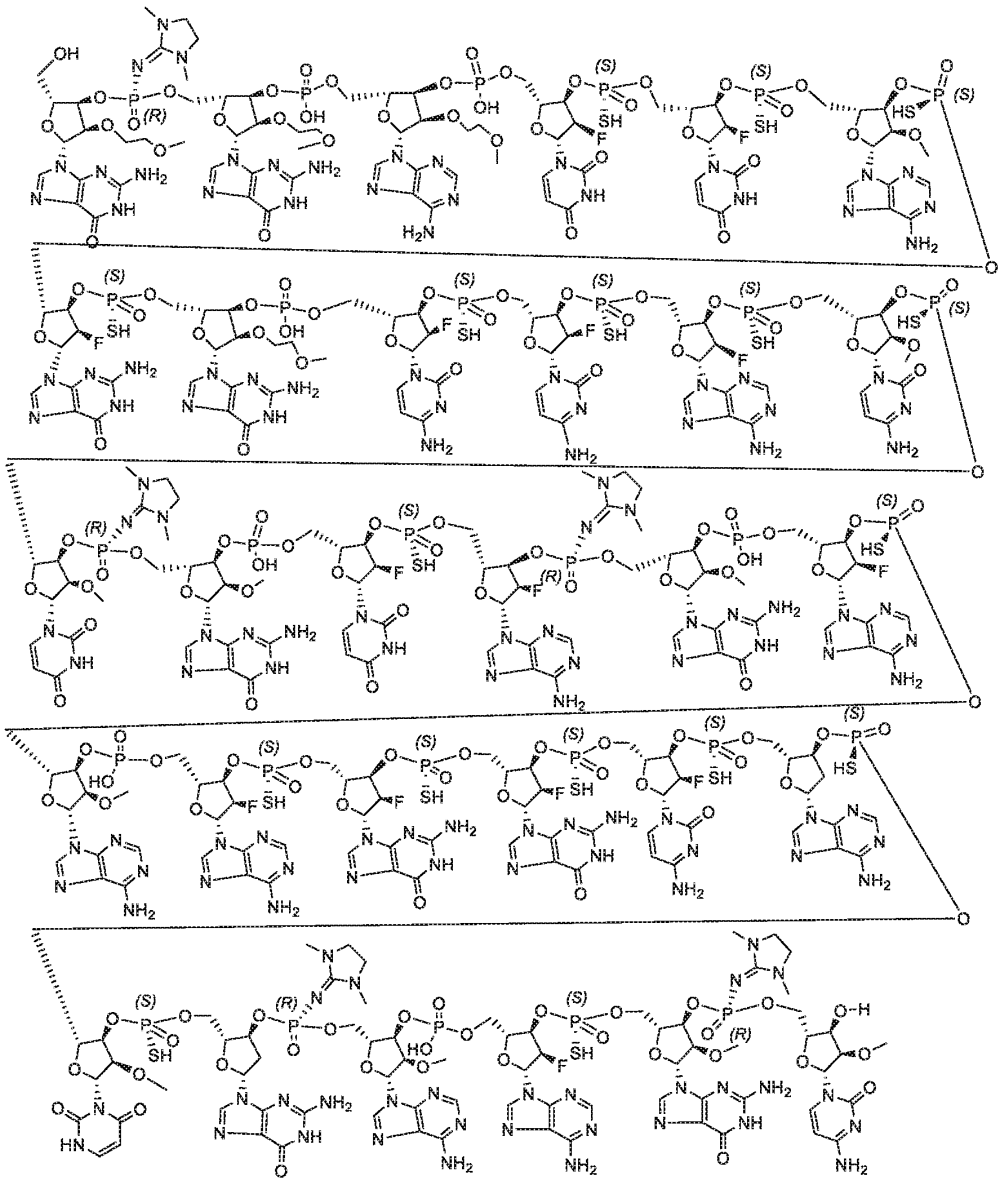
A-4



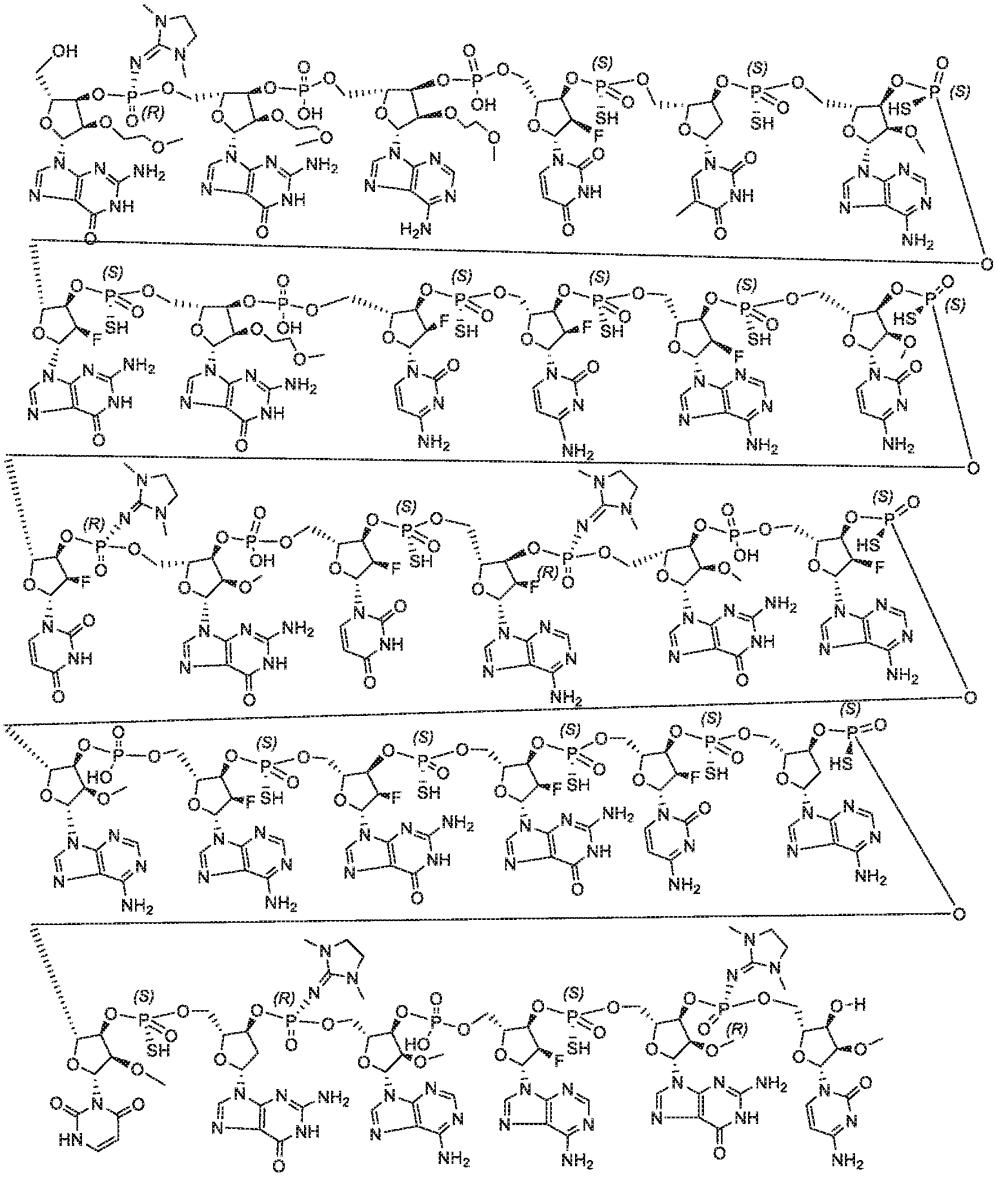
B-1



B-2



B-3



B-4

First Domains

[00233] As described herein, in some embodiment, an oligonucleotide comprises a first domain and a second domain. In some embodiments, an oligonucleotide consists of a first domain and a second domain. Certain embodiments are described below as examples.

[00234] In some embodiments, a first domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a

first domain has a length of about 5-30 nucleobases. In some embodiments, a first domain has a length of about 10-30 nucleobases. In some embodiments, a first domain has a length of about 10-20 nucleobases. In some embodiments, a first domain has a length of about 13-16 nucleobases. In some embodiments, a first domain has a length of 10 nucleobases. In some embodiments, a first domain has a length of 11 nucleobases. In some embodiments, a first domain has a length of 12 nucleobases. In some embodiments, a first domain has a length of 13 nucleobases. In some embodiments, a first domain has a length of 14 nucleobases. In some embodiments, a first domain has a length of 15 nucleobases. In some embodiments, a first domain has a length of 16 nucleobases. In some embodiments, a first domain has a length of 17 nucleobases. In some embodiments, a first domain has a length of 18 nucleobases. In some embodiments, a first domain has a length of 19 nucleobases. In some embodiments, a first domain has a length of 20 nucleobases.

[00235] In some embodiments, a first domain is about, or at least about, 5-95%, 10%-90%, 20%-80%, 30%-70%, 40%-70%, 40%-60%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% of an oligonucleotide. In some embodiments, a percentage is about 30%-80%. In some embodiments, a percentage is about 30%-70%. In some embodiments, a percentage is about 40%-60%. In some embodiments, a percentage is about 20%. In some embodiments, a percentage is about 25%. In some embodiments, a percentage is about 30%. In some embodiments, a percentage is about 35%. In some embodiments, a percentage is about 40%. In some embodiments, a percentage is about 45%. In some embodiments, a percentage is about 50%. In some embodiments, a percentage is about 55%. In some embodiments, a percentage is about 60%. In some embodiments, a percentage is about 65%. In some embodiments, a percentage is about 70%. In some embodiments, a percentage is about 75%. In some embodiments, a percentage is about 80%. In some embodiments, a percentage is about 85%. In some embodiments, a percentage is about 90%.

[00236] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches exist in a first domain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches. In some embodiments, there are 10 mismatches.

[00237] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles exist in a first domain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 wobble. In some embodiments, there are 2 wobbles. In some embodiments, there are 3 wobbles. In some embodiments, there are 4 wobbles. In some embodiments, there are 5 wobbles. In some embodiments, there are 6 wobbles. In some embodiments, there are 7 wobbles. In some embodiments, there are 8 wobbles. In some embodiments, there are 9 wobbles. In some embodiments, there are 10 wobbles.

[00238] In some embodiments, duplexes of oligonucleotides and target nucleic acids in a first domain

region comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00239] In some embodiments, a first domain is fully complementary to a target nucleic acid.

[00240] In some embodiments, a first domain comprises one or more modified nucleobases.

[00241] In some embodiments, a second domain comprises one or more sugars comprising two 2'-H (e.g., natural DNA sugars). In some embodiments, a second domain comprises one or more sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a first domain comprises one or more modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar).

[00242] In some embodiments, a first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars. In some embodiments, a first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars with 2'-F modification. In some embodiments, a first domain comprises about 2-50 (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., 2-40, 2-30, 2-25, 2-20, 2-15, 2-10, 3-40, 3-30, 3-25, 3-20, 3-15, 3-10, 4-40, 4-30, 4-25, 4-20, 4-15, 4-10, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 6-40, 6-30, 6-25, 6-20, 6-15, 6-10, 7-40, 7-30, 7-25, 7-20, 7-15, 7-10, 8-40, 8-30, 8-25, 8-20, 8-15, 8-10, 9-40, 9-30, 9-25, 9-20, 9-15, 9-10, 10-40, 10-30, 10-25, 10-20, 10-15, about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) consecutive modified sugars with 2'-F modification. In some embodiments, a first domain comprises 2 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 3 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 4 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 5 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 6 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 7 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 8 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 9 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises 10 consecutive 2'-F modified sugars. In some embodiments, a first domain comprises two or more 2'-F modified sugar blocks, wherein each sugar in a 2'-F modified sugar block

is independently a 2'-F modified sugar. In some embodiments, each 2'-F modified sugar block independently comprises or consists of 2, 3, 4, 5, 6, 7, 8, 9, or 10 consecutive 2'-F modified sugars as described herein. In some embodiments, two consecutive 2'-F modified sugar blocks are independently separated by a separating block which separating block comprises one or more sugars that are independently not 2'-F modified sugars. In some embodiments, each sugar in a separating block is independently not 2'-F modified. In some embodiments, two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) or all sugars in a separating block are independently not 2'-F modified. In some embodiments, a separating block comprises one or more bicyclic sugars (e.g., LNA sugar, cEt sugar, etc.) and/or one or more 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, a separating block comprises one or more 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, two or more non-2'-F modified sugars are consecutive. In some embodiments, two or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.) are consecutive. In some embodiments, a separating block comprises two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, a separating block comprises two or more (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) consecutive 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic (e.g., 2'-OMe, 2'-MOE, etc.). In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE sugar. In some embodiments, a separating block comprises one or more 2'-F modified sugars. In some embodiments, none of 2'-F modified sugars in a separating block are next to each other. In some embodiments, a separating block contain no 2'-F modified sugars. In some embodiments, each sugar in a separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each sugar in each separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each sugar in a separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in each separating block is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a separating block is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in each separating block is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in a separating block is independently a 2'-OMe modified sugar. In some embodiments, each sugar in a separating block is independently a 2'-MOE modified sugar. In some embodiments, a separating block comprises a 2'-OMe sugar and 2'-MOE modified sugar. In some embodiments, each 2'-F block and each separating block independently contains 1, 2, 3, 4, or 5 nucleosides. In some embodiments, each 2'-F block and each separating block independently contains 1, 2, or 3 nucleosides.

[00243] In some embodiments, about 5%-100%, (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%,

65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a first domain are independently a modified sugar. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a first domain are independently a 2'-F modified sugar. In some embodiments, a percentage is at least about 40%. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 60%. In some embodiments, a percentage is about or no more than about 70%. In some embodiments, a percentage is about or no more than about 80%. In some embodiments, a percentage is about or no more than about 90%.

[00244] In some embodiments, a first domain comprises no bicyclic sugars or 2'-OR modified sugars wherein R is not –H. In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H. In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-OR modified sugars wherein R is not –H. In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-OR modified sugars wherein R is optionally substituted C_{1-10} aliphatic. In some embodiments, levels of bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H, individually or combined, are relatively low compared to level of 2'-F modified sugars. In some embodiments, levels of bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H, individually or combined, are about 10%–80% (e.g., about 10%-75%, 10-70%, 10%-65%, 10%-60%, 10%-50%, about 20%-60%, about 30%-60%, about 20%-50%, about 30%-50%, about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, or 60%, etc.). In some embodiments, levels of 2'-OR modified sugars wherein R is not –H combined (e.g., 2'-OMe and 2'-MOE modified sugars combined, if any) are about 10–70% (e.g., about 10%-60%, 10%-50%, about 20%-60%, about 30%-60%, about 20%-50%, about 30-50%, about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, or 60%, etc.). In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first domain

comprises 2'-OMe. In some embodiments, no more than about 50% of sugars in a first domain comprises 2'-OMe. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 50% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 40% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 30% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 25% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 20% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, no more than about 10% of sugars in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, as described herein, 2'-OR is 2'-MOE. In some embodiments, as described herein, 2'-OR is 2'-MOE or 2'-OMe. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-$N(R)_2$ modification. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-NH_2 modification. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) bicyclic sugars, e.g., LNA sugars. In some embodiments, a first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars). In some embodiments, a number of 5'-end sugars in a first domain are independently 2'-OR modified sugars, wherein R is not −H. In some embodiments, a number of (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more) 5'-end sugars in a first domain are independently 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the first about 1-10, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, sugars from the 5'-end of a first domain are independently 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the first one is 2'-OR modified. In some embodiments, the first two are independently 2'-OR modified. In some embodiments, the first three are independently 2'-OR modified. In some embodiments, the first four are independently 2'-OR modified. In some embodiments, the first five are independently 2'-OR modified. In some embodiments, all 2'-OR modification in a domain (e.g., a first domain), a subdomain (e.g., a first subdomain), or an oligonucleotide are the same. In some embodiments, 2'-OR is 2'-MOE. In some embodiments, 2'-OR is 2'-OMe.

[00245] In some embodiments, no sugar in a first domain comprises 2'-OR. In some embodiments, no sugar in a first domain comprises 2'-OMe. In some embodiments, no sugar in a first domain comprises 2'-MOE. In some embodiments, no sugar in a first domain comprises 2'-MOE or 2'-OMe. In some embodiments, no sugar in a first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a first domain comprises 2'-F.

[00246] In some embodiments, about 40-70% (e.g., about 40%-70%, 40%-60%, 50%-70%, 50%-60%, etc., or about 40%, 45%, 50%, 55%, 60%, 65%, 70%, etc.) of sugars in a first domain are 2'-F modified, and about 10%-60% (e.g., about 10%-50%, 20%-60%, 30%-60%, 30%-50%, 40%-50%, etc., or about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, or 60%) of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars (e.g., LNA sugars, cEt sugars, etc.). In some embodiments, about 20%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 25%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 30%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 35%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 40%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 50%-60% of sugars in a first domain are 2'-F modified. In some embodiments, about 50%-70% of sugars in a first domain are 2'-F modified. In some embodiments, about 20%-60% of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars. In some embodiments, about 30%-60% of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars. In some embodiments, about 40%-60% of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars. In some embodiments, about 30%-50% of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars. In some embodiments, about 40%-50% of sugars in a first domain are independently 2'-OR modified wherein R is not −H or bicyclic sugars. In some embodiments, each of the sugars in a first domain that are independently 2'-OR modified wherein R is not −H or bicyclic sugars is independently a 2'-OR modified sugar wherein R is not −H. In some embodiments, each of them is independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, each of them is independently a 2'-OR modified sugar wherein R is C_{1-6} alky. In some embodiments, each of them is independently a 2'-OMe or 2'-MOE modified sugar.

[00247] In some embodiments, a first domain comprise about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 − about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a first domain are modified internucleotidic linkages. In some embodiments, each internucleotidic linkage in a first domain is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PS internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified or

chiral internucleotidic linkage is a PN internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a neutral internucleotidic linkage, e.g., n001. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a first domain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a first domain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a first domain is chirally controlled. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a first domain is *Sp*. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) phosphorothioate internucleotidic linkages in a first domain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.)

of chiral internucleotidic linkages in a first domain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a first domain is *Sp*. In some embodiments, the number is one or more. In some embodiments, the number is 2 or more. In some embodiments, the number is 3 or more. In some embodiments, the number is 4 or more. In some embodiments, the number is 5 or more. In some embodiments, the number is 6 or more. In some embodiments, the number is 7 or more. In some embodiments, the number is 8 or more. In some embodiments, the number is 9 or more. In some embodiments, the number is 10 or more. In some embodiments, the number is 11 or more. In some embodiments, the number is 12 or more. In some embodiments, the number is 13 or more. In some embodiments, the number is 14 or more. In some embodiments, the number is 15 or more. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, each internucleotidic linkages linking two first domain nucleosides is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage of a first domain is bonded to two nucleosides of the first domain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a first domain and a nucleoside in a second domain may be properly considered an internucleotidic linkage of a first domain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a first domain and a nucleoside in a second domain is a modified internucleotidic linkage; in some embodiments, it is a chiral internucleotidic linkage; in some embodiments, it is chirally controlled; in some embodiments, it is *Rp*; in some embodiments, it is *Sp*. In many embodiments, it was observed that a high percentage (e.g., relative to *Rp* internucleotidic linkages and/or natural phosphate linkages) of *Sp* internucleotidic linkages provide improved properties and/or activities, e.g., high stability

and/or high adenosine editing activity.

[00248] In some embodiments, a first domain comprises a certain level of *R*p internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in a first domain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in a first domain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in a first domain. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 1-5, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *R*p chiral internucleotidic linkages. In some embodiments, the number is about or no more than about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the

number is about or no more than about 3. In some embodiments, the number is about or no more than about 4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10.

[00249] In some embodiments, each phosphorothioate internucleotidic linkage in a first domain is independently chirally controlled. In some embodiments, each is independently *Sp* or *Rp*. In some embodiments, a high level is *Sp* as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a first domain is chirally controlled and is *Sp*.

[00250] In some embodiments, as illustrated in certain examples, a first domain comprises one or more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Rp*. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Sp*. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in a first domain is about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, it is about 1. In some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in a first domain are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more consecutive non-negatively charged internucleotidic linkages, are at the 5'-end of a first domain. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first domain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first domain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first domain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first domain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first domain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first domain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides

of a first domain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first domain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first domain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first domain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage such as n001. In some embodiments, the first two nucleosides of a first domain are the first two nucleosides of an oligonucleotide.

[00251] In some embodiments, a first domain comprises one or more PO internucleotidic linkages. In some embodiments, a first domain comprises one or more natural phosphate linkages. In some embodiments, a first domain contains no natural phosphate linkages. In some embodiments, one or more 2'-OR modified sugars wherein R is not −H are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-OMe modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-MOE modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, each 2'-MOE modified sugar is independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-OR modified sugars wherein R is not −H are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-OMe modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-MOE modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) internucleotidic linkages bonded to two 2'-OR modified sugars are independently natural phosphate linkages. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) internucleotidic linkages bonded to two 2'-OMe or 2'-MOE modified sugars are independently natural phosphate linkages.

[00252] In some embodiments, in an oligonucleotide of the present disclosure or a portion thereof, e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc., each internucleotidic linkage bonded to two 2'-F modified sugars is independently a modified internucleotidic linkage. In some embodiments, it is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage such as a phosphoryl guanidine internucleotidic linkage like n001. In some embodiments, it is independently a *Sp* phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage such as a phosphoryl guanidine internucleotidic linkage like n001. In some embodiments, it is independently a *Sp* phosphorothioate internucleotidic linkage or a *Rp* phosphoryl guanidine

internucleotidic linkage like *Rp* n001. In some embodiments, each phosphorothioate internucleotidic linkage bonded to two 2'-F modified sugars is independently *Sp*.

[00253] In some embodiments, a first domain recruits, promotes or contribute to recruitment of, a protein such as an ADAR protein (e.g., ADAR1, ADAR2, etc.). In some embodiments, a first domain recruits, or promotes or contribute to interactions with, a protein such as an ADAR protein. In some embodiments, a first domain contacts with a RNA binding domain (RBD) of ADAR. In some embodiments, a first domain does not substantially contact with a second RBD domain of ADAR. In some embodiments, a first domain does not substantially contact with a catalytic domain of ADAR which has a deaminase activity. In some embodiments, various nucleobases, sugars and/or internucleotidic linkages may interact with one or more residues of proteins, e.g., ADAR proteins.

Second Domains

[00254] As described herein, in some embodiment, an oligonucleotide comprises a first domain and a second domain from 5' to 3'. In some embodiments, an oligonucleotide consists of a first domain and a second domain. Certain embodiments of a second domain are described below as examples. In some embodiments, a second domain comprise a nucleoside opposite to a target adenosine to be modified (e.g., conversion to I).

[00255] In some embodiments, a second domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a second domain has a length of about 5-30 nucleobases. In some embodiments, a second domain has a length of about 10-30 nucleobases. In some embodiments, a second domain has a length of about 10-20 nucleobases. In some embodiments, a second domain has a length of about 5-15 nucleobases. In some embodiments, a second domain has a length of about 13-16 nucleobases. In some embodiments, a second domain has a length of about 1-7 nucleobases. In some embodiments, a second domain has a length of 10 nucleobases. In some embodiments, a second domain has a length of 11 nucleobases. In some embodiments, a second domain has a length of 12 nucleobases. In some embodiments, a second domain has a length of 13 nucleobases. In some embodiments, a second domain has a length of 14 nucleobases. In some embodiments, a second domain has a length of 15 nucleobases. In some embodiments, a second domain has a length of 16 nucleobases. In some embodiments, a second domain has a length of 17 nucleobases. In some embodiments, a second domain has a length of 18 nucleobases. In some embodiments, a second domain has a length of 19 nucleobases. In some embodiments, a second domain has a length of 20 nucleobases.

[00256] In some embodiments, a second domain is about, or at least about, 5-95%, 10%-90%, 20%-80%, 30%-70%, 40%-70%, 40%-60%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% of an oligonucleotide. In some embodiments, a percentage is about 30%-80%. In some embodiments, a percentage is about 30%-70%. In some embodiments, a percentage is about 40%-60%. In some embodiments, a percentage is about 20%. In some embodiments, a percentage is about 25%. In some embodiments, a percentage is about 30%. In some embodiments, a percentage is about 35%.

In some embodiments, a percentage is about 40%. In some embodiments, a percentage is about 45%. In some embodiments, a percentage is about 50%. In some embodiments, a percentage is about 55%. In some embodiments, a percentage is about 60%. In some embodiments, a percentage is about 65%. In some embodiments, a percentage is about 70%. In some embodiments, a percentage is about 75%. In some embodiments, a percentage is about 80%. In some embodiments, a percentage is about 85%. In some embodiments, a percentage is about 90%.

[00257] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches exist in a second domain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches. In some embodiments, there are 10 mismatches.

[00258] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles exist in a second domain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 wobble. In some embodiments, there are 2 wobbles. In some embodiments, there are 3 wobbles. In some embodiments, there are 4 wobbles. In some embodiments, there are 5 wobbles. In some embodiments, there are 6 wobbles. In some embodiments, there are 7 wobbles. In some embodiments, there are 8 wobbles. In some embodiments, there are 9 wobbles. In some embodiments, there are 10 wobbles.

[00259] In some embodiments, duplexes of oligonucleotides and target nucleic acids in a second domain region comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00260] In some embodiments, a second domain is fully complementary to a target nucleic acid.

[00261] In some embodiments, a second domain comprises one or more modified nucleobases.

[00262] In some embodiments, a second domain comprise a nucleoside opposite to a target adenosine, e.g., when the oligonucleotide forms a duplex with a target nucleic acid. In some embodiments, an opposite nucleobase is optionally substituted or protected U, or is an optionally substituted or protected tautomer of U. In some embodiments, an opposite nucleobase is U.

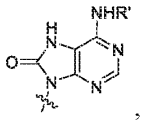
[00263] In some embodiments, an opposite nucleobase has weaker hydrogen bonding with a target adenine of a target adenosine compared to U. In some embodiments, an opposite nucleobase forms fewer hydrogen bonds with a target adenine of a target adenosine compared to U. In some embodiments, an opposite nucleobase forms one or more hydrogen bonds with one or more amino acid residues of a protein, e.g., ADAR,

which residues form one or more hydrogen bonds with U opposite to a target adenosine. In some embodiments, an opposite nucleobase forms one or more hydrogen bonds with each amino acid residue of ADAR that forms one or more hydrogen bonds with U opposite to a target adenosine. In some embodiments, by weakening hydrogen boding with a target A and/or maintaining or enhancing interactions with proteins such as ADAR1, ADAR2, etc., certain opposite nucleobase facilitate and/or promote adenosine modification, e.g., by ADAR proteins such as ADAR1 and ADAR2.

[00264] In some embodiments, an opposite nucleobase is optionally substituted or protected C, or is an optionally substituted or protected tautomer of C. In some embodiments, an opposite nucleobase is C. In some embodiments, an opposite nucleobase is optionally substituted or protected A, or is an optionally substituted or protected tautomer of A. In some embodiments, an opposite nucleobase is A. In some embodiments, an opposite nucleobase is optionally substituted or protected nucleobase of pseudoisocytosine, or is an optionally substituted or protected tautomer of the nucleobase of pseudoisocytosine. In some embodiments, an opposite nucleobase is the nucleobase of pseudoisocytosine.

[00265] In some embodiments, a nucleoside, e.g., a nucleoside opposite to a target adenosine (may also be referred to as "an opposite nucleoside") is abasic as described herein (e.g., having the structure of L010, L012, L028, etc.).

[00266] Many useful embodiments of modified nucleobases, e.g., for opposite nucleobases, are also described below. In some embodiments, as described herein (e.g., in various oligonucleotides), the present disclosure provides oligonucleotides comprising a nucleobase, e.g., of a nucleoside opposite to a target nucleoside such as A (N_0), N_1, N_{-1}, etc., which is or comprises A, T, C, G, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], zdnp or a nucleobase described in Table BA-1. In some embodiments, as described herein (e.g., in various oligonucleotides), the present disclosure provides oligonucleotides comprising a nucleobase, e.g., of a nucleoside opposite to a target nucleoside such as A, which is or comprises b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b001A, b002A, b003A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], and zdnp. In some embodiments, as described herein (e.g., in various oligonucleotides), the present disclosure provides oligonucleotides comprising a nucleobase, e.g., of a nucleoside opposite to a target nucleoside such as A, which is or comprises C, A, b007U, b001U, b001A, b002U, b001C, b003U, b002C, b004U, b003C, b005U, b002I, b006U, b003I, b008U, b009U, b002A, b003A, b001G, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], or zdnp. In some embodiments, a nucleobase is C. In some embodiments, a nucleobase is A. In some embodiments, a nucleobase is hypoxanthine. In some embodiments, a nucleobase is b002I. In some

embodiments, a nucleobase is b003I. In some embodiments, a nucleobase is b004I. In some embodiments, a nucleobase is b014I. In some embodiments, a nucleobase is b001C. In some embodiments, a nucleobase is b002C. In some embodiments, a nucleobase is b003C. In some embodiments, a nucleobase is b004C. In some embodiments, a nucleobase is b005C. In some embodiments, a nucleobase is b006C. In some embodiments, a nucleobase is b007C. In some embodiments, a nucleobase is b008C. In some embodiments, a nucleobase is b009C. In some embodiments, a nucleobase is b001U. In some embodiments, a nucleobase is b002U. In some embodiments, a nucleobase is b003U. In some embodiments, a nucleobase is b004U. In some embodiments, a nucleobase is b005U. In some embodiments, a nucleobase is b006U. In some embodiments, a nucleobase is b007U. In some embodiments, a nucleobase is b008U. In some embodiments, a nucleobase is b009U. In some embodiments, a nucleobase is b011U. In some embodiments, a nucleobase is b012U. In some embodiments, a nucleobase is b013U. In some embodiments, a nucleobase is b014U. In some embodiments, a nucleobase is b015U. In some embodiments, a nucleobase is b001A. In some embodiments, a nucleobase is b002A. In some embodiments, a nucleobase is b003A. In some embodiments, a nucleobase is b004A. In some embodiments, a nucleobase is b005A. In some embodiments, a nucleobase is b006A. In some embodiments, a nucleobase is b007A. In some embodiments, a nucleobase is b001G. In some embodiments, a nucleobase is b002G. In some embodiments, a nucleobase is [3nT]. In some embodiments, a nucleobase is [3ne5U]. In some embodiments, a nucleobase is [3nfl5U]. In some embodiments, a nucleobase is [3npry5U]. In some embodiments, a nucleobase is [3ncn5U]. In some embodiments, a nucleobase is [nathp6o8A]. In some embodiments, a nucleobase is [ipr6o8A]. In some embodiments, a nucleobase is [c7In]. In some embodiments, a nucleobase is [c39z48In]. In some embodiments, a nucleobase is [z2c3In]. In some embodiments, a nucleobase is [z5C]. In some embodiments, a nucleobase is zdnp. In some embodiments, a nucleobase is selected from Table BA-1. In some embodiments, such a nucleobase is in N_0. In some embodiments, such a nucleobase is in N_1. In some embodiments, such a nucleobase is in N_{-1}. In some embodiments, as those skilled in the art appreciate, a nucleobase is protected, e.g., for oligonucleotide synthesis. For example, in some embodiments, a nucleobase is protected b001A having the structure of , wherein R' is as described herein. In some embodiments, R' is −C(O)R. In some embodiments, R' is −C(O)Ph.

[00267] In some embodiments, it was observed that various modified nucleobases, e.g., b001A, b008U, etc., can provide improved adenosine editing efficiency when compared to a reference nucleobase (e.g., under comparable conditions including, e.g., in otherwise identical oligonucleotides, assessed in identical or comparable assays, etc.). In some embodiments, a reference nucleobase is U. In some embodiments, a reference nucleobase is T. In some embodiments, a reference nucleobase is C.

Certain modified nucleobases

[00268] In some embodiments, BA is or comprises Ring BA or a tautomer thereof, wherein Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms. In some embodiments, Ring BA is or comprises an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, Ring BA is saturated. In some embodiments, Ring BA comprises one or more unsaturation. In some embodiments, Ring BA is partially unsaturated. In some embodiments, Ring BA is aromatic.

[00269] In some embodiments, BA is or comprises Ring BA, wherein Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms. In some embodiments, Ring BA is or comprises an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, Ring BA is saturated. In some embodiments, Ring BA comprises one or more unsaturation. In some embodiments, Ring BA is partially unsaturated. In some embodiments, Ring BA is aromatic.

[00270] In some embodiments, BA is or comprises Ring BA. In some embodiments, BA is Ring BA. In some embodiments, BA is or comprises a tautomer of Ring BA. In some embodiments, BA is a tautomer of Ring BA.

[00271] In some embodiments, structures of the present disclosure contain one or more optionally substituted rings (e.g., Ring BA, −Cy−, Ring BA^A, R, formed by R groups taken together, etc.). In some embodiments, a ring is an optionally substituted C_{3-30}, C_{3-20}, C_{3-15}, C_{3-10}, C_{3-9}, C_{3-8}, C_{3-7}, C_{3-6}, C_{5-50}, C_{5-20}, C_{5-15}, C_{5-10}, C_{5-9}, C_{5-8}, C_{5-7}, C_{5-6}, or 3-30 (e.g., 3-30, 3-20, 3-15, 3-10, 3-9, 3-8, 3-7, 3-6, 5-50, 5-20, 5-15, 5-10, 5-9, 5-8, 5-7, 5-6, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, etc.) membered monocyclic, bicyclic or polycyclic ring having 0-10 (e.g., 1-10, 1-5, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) heteroatoms. In some embodiments, a ring is an optionally substituted 3-10 membered monocyclic or bicyclic, saturated, partially saturated or aromatic ring having 0-3 heteroatoms. In some embodiments, a ring is substituted. In some embodiments, a ring is not substituted. In some embodiments, a ring is 3, 4, 5, 6, 7, 8, 9, or 10 membered. In some embodiments, a ring is 5, 6, or7-membered. In some embodiments, a ring is 5-membered. In some embodiments, a ring is 6-membered. In some embodiments, a ring is 7-membered. In some embodiments, a ring is monocyclic. In some embodiments, a ring is bicyclic. In some embodiments, a ring is polycyclic. In some embodiments, a ring is saturated. In some embodiments, a ring contains at least one unsaturation. In some embodiments, a ring is partially unsaturated. In some embodiments, a ring is aromatic. In some embodiments, a ring has 0-5 heteroatoms. In some embodiments, a ring has 1-5 heteroatoms. In some embodiments, a ring has one or more heteroatoms. In some embodiments, a ring has 1 heteroatom. In some embodiments, a ring has 2 heteroatoms. In some embodiments, a ring has 3 heteroatoms. In some embodiments, a ring has 4 heteroatoms. In some embodiments, a ring has 5 heteroatoms. In some embodiments, a heteroatom is nitrogen. In some embodiments, a heteroatom is oxygen. In some embodiments, a ring is substituted, e.g., substituted with one or more alkyl groups and optionally one or more other substituents as described herein. In some embodiments, a substituent is methyl.

[00272] In some embodiments, each monocyclic ring unit of a monocyclic, bicyclic, or polycyclic ring of the present disclosure (e.g., Ring BA, –Cy–, Ring BA^A, R, formed by R groups taken together, etc.) is independently an optionally substituted 5-7 membered, saturated, partially unsaturated or aromatic ring having 0-5 heteroatoms. In some embodiments, one or more monocyclic units independently comprise one or more unsaturation. In some embodiments, one or more monocyclic units are saturated. In some embodiments, one or more monocyclic units are partially saturated. In some embodiments, one or more monocyclic units are aromatic. In some embodiments, one or more monocyclic units independently have 1-5 heteroatoms. In some embodiments, one or more monocyclic units independently have at least one nitrogen atom. In some embodiments, each monocyclic unit is independently 5- or 6-membered. In some embodiments, a monocyclic unit is 5-membered. In some embodiments, a monocyclic unit is 5-membered and has 1-2 nitrogen atom. In some embodiments, a monocyclic unit is 6-membered. In some embodiments, a monocyclic unit is 6-membered and has 1-2 nitrogen atom. Rings and monocyclic units thereof are optionally substituted unless otherwise specified.

[00273] Without the intention to be limited by any particular theory, the present disclosure recognizes that in some embodiment, structures of nucleobases (e.g. BA) can impact interactions with proteins (e.g., ADAR proteins such as ADAR1, ADAR2, etc.). In some embodiments, provided oligonucleotides comprise nucleobases that can facility interaction of an oligonucleotide with an enzyme, e.g., ADAR1. In some embodiments, provided oligonucleotides comprise nucleobases that may reduce strength of base pairing (e.g., compared to A–T/U or C–G). In some embodiments, the present disclosure recognizes that by maintaining and/or enhancing interactions (e.g., hydrogen bonding) of a first nucleobase with a protein (e.g., an enzyme like ADAR1) and/or reducing interactions (e.g., hydrogen bonding) of a first nucleobase with its corresponding nucleobase (e.g., A) on the other strand in a duplex, modification of the corresponding nucleobase by a protein (e.g., an enzyme like ADAR1) can be significantly improved. In some embodiments, the present disclosure provides oligonucleotides comprises such a first nucleobase (e.g., various embodiments of BA described herein). Exemplary embodiments of such as a first nucleobase are as described herein. In some embodiments, when an oligonucleotide comprising such a first nucleobase is aligned with another nucleic acid for maximum complementarity, the first nucleobase is opposite to A. In some embodiments, such an A opposite to the first nucleobase, as exemplified in many embodiments of the present disclosure, can be efficiently modified using technologies of the present disclosure.

[00274] In some embodiments, Ring BA comprises a moiety $=\!=\!=X^2=\!=\!=X^3=\!=\!=$, wherein each variable is independently as described herein. In some embodiments, Ring BA comprises a moiety $=\!=\!=X^2=\!=\!=X^3=\!=\!=X^4=\!=\!=$, wherein each variable is independently as described herein. In some embodiments, Ring BA comprises a moiety $-X^1(=\!=\!=)=\!=\!=X^2=\!=\!=X^3=\!=\!=$, wherein each variable is independently as described herein. In some embodiments, Ring BA comprises a moiety $-X^1(=\!=\!=)=\!=\!=X^2=\!=\!=X^3=\!=\!=X^4=\!=\!=$, wherein each variable is independently as described herein. In some embodiments, X^1 is bonded to a sugar. In some embodiments, X^1 is –N(–)–. In some embodiments, X^1 is –C(=)–. In some embodiments, X^2 is –C(O)–. In some embodiments,

X^3 is –NH–. In some embodiments, X^4 is not –C(O)–. In some embodiments, X^4 is –C(O)–, and forms an intramolecular hydrogen bond, e.g., with a moiety of the same nucleotidic unit (e.g., within the same BA unit (e.g., with a hydrogen bond donor (e.g., –OH, SH, etc.) of X^5). In some embodiments, X^4 is –C(=NH)–. In some embodiments, Ring BA comprises a moiety ===$X^{4'}$===$X^{5'}$===, wherein each variable is independently as described herein. In some embodiments, $X^{4'}$ is –C(O)–. In some embodiments, $X^{5'}$ is –NH–.

[00275] In some embodiments, BA is optionally substituted or protected C or a tautomer thereof. In some embodiments, BA is optionally substituted or optionally protected C. In some embodiments, BA is an optionally substituted or optionally protected tautomer of C. In some embodiments, BA is C. In some embodiments, BA is substituted C. In some embodiments, BA is protected C. In some embodiments, BA is an substituted tautomer of C. In some embodiments, BA is an protected tautomer of C.

[00276] In some embodiments, Ring BA has the structure of formula BA-I:



BA-I

wherein:

Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic, saturated, partially saturated or aromatic ring having 1-10 heteroatoms;

each === is independent a single or double bond;

X^1 is –N(–)– or –C(–)=;

X^2 is –C(W^{X2})–, –C(R^{B2})=, –C(OR^{B2})=, –N= or optionally substituted –CH=, wherein R^{B2} is halogen, –CN, –NO_2, or –L^{B2}–R', and W^{X2} is O, S or Se;

X^3 is –C(R^{B3})=, –N(R^{B3})–, –N= or optionally substituted –NH– or –CH=, wherein R^{B3} is halogen, –CN, –NO_2, or –L^{B3}–R';

X^4 is –C(R^{B4})=, –C(–N(R^{B4})$_2$)=, –C(R^{B4})$_2$–, –C(W^{X4})–, –C(=NR^{B4})– or optionally substituted –CH= or –CH_2–, wherein each R^{B4} is independently halogen, –CN, –NO_2, or –L^{B4}–R^{B41}, or two R^{B4} on the same atom are taken together to form =O, =C(–L^{B4}–R^{B41})$_2$, =N–L^{B4}– R^{B41}, or optionally substituted =CH_2 or =NH, wherein each R^{B41} is independently R', and W^{X4} is O, S or Se;

each of L^{B2}, L^{B3}, and L^{B4} is independently L^B;

each L^B is independently a covalent bond, or an optionally substituted bivalent C_{1-10} saturated or partially unsaturated chain having 0-6 heteroatoms, wherein one or more methylene unit is optionally and independently replaced with –Cy–, –O–, –S–, –N(R')–, –C(O)–, –C(S)–, –C(NR')–, –C(O)N(R')–, –N(R')C(O)N(R')–, –N(R')C(O)O–, –S(O)–, –S(O)$_2$–, –S(O)$_2$N(R')–, –C(O)S–, or –C(O)O–;

each –Cy– is independently an optionally substituted, 3-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms;

each R' is independently –R, –C(O)R, –C(O)OR, –C(O)N(R)$_2$, or –SO_2R; and

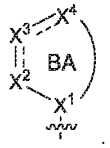
each R is independently –H, or an optionally substituted group selected from C_{1-20} aliphatic, C_{1-20} heteroaliphatic having 1-10 heteroatoms, C_{6-20} aryl, C_{6-20} arylaliphatic, C_{6-20} arylheteroaliphatic having 1-10 heteroatoms, 5-20 membered heteroaryl having 1-10 heteroatoms, and 3-20 membered heterocyclyl having 1-10 heteroatoms, or:

two R groups are optionally and independently taken together to form a covalent bond, or:

two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-20 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms; or:

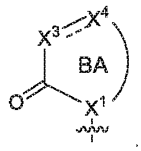
two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms.

[00277] In some embodiments, Ring BA (e.g., one of formula BA-I) has the structure of formula BA-I-a:



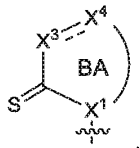
BA-I-a

[00278] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, etc.)has the structure of formula BA-I-b:



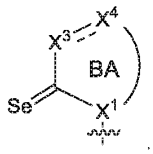
BA-I-b

[00279] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, etc.)has the structure of formula BA-I-c:



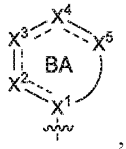
BA-I-c

[00280] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, etc.)has the structure of formula BA-I-d:



BA-I-d

[00281] In some embodiments, Ring BA (e.g., one of formula BA-I) has the structure of formula BA-II:



BA-II

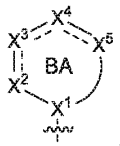
wherein:

X^5 is $-C(R^{B5})_2-$, $-N(R^{B5})-$, $-C(R^{B5})=$, $-C(W^{X5})-$, $-N=$ or optionally substituted $-CH_2-$, $-NH-$ or $-CH=$, wherein each R^{B5} is independently halogen, $-CN$, $-NO_2$, or $-L^{B5}-R^{B51}$, wherein R^{B51} is $-R'$, $-N(R')_2$, $-OR'$, or $-SR'$, and W^{X5} is O, S, or Se;

L^{B5} is L^B; and

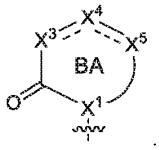
each other variable is independently as described herein.

[00282] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-II, etc.) has the structure of formula BA-II-a:



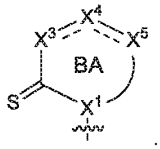
BA-II-a

[00283] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, etc.) has the structure of formula BA-II-b:



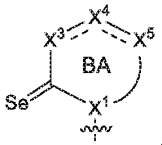
BA-II-b

[00284] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, etc.) has the structure of formula BA-II-b:



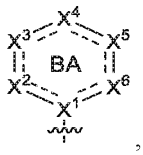
BA-II-c

[00285] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, etc.) has the structure of formula BA-II-b:



BA-II-d

[00286] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-II, etc.) has the structure of formula BA-III:



BA-III

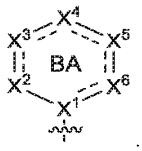
wherein:

X^6 is $-C(R^{B6})=$, $-C(OR^{B6})=$, $-C(R^{B6})_2-$, $-C(W^{X6})-$, $-N=$ or optionally substituted $-CH=$ or $-CH_2-$, wherein each R^{B6} is independently halogen, $-CN$, $-NO_2$, or $-L^{B6}-R^{B61}$, or two R^{B6} on the same atom are taken together to form $=O$, $=C(-L^{B6}-R^{B61})_2$, $=N-L^{B6}-R^{B61}$, or optionally substituted $=CH_2$ or $=NH$, wherein each R^{B61} is independently R', and W^{X6} is O, S, or Se;

L^{B6} is L^B; and

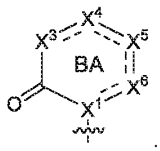
each other variable is independently as described herein.

[00287] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-II, BA-II-a, BA-III, etc.) has the structure of formula BA-III-a:



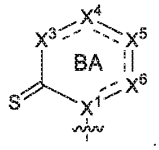
BA-III-a

[00288] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, BA-II-b, BA-III, BA-III-a, etc.) has the structure of formula BA-III-b:



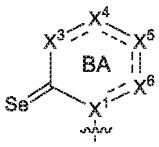
BA-III-b

[00289] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, BA-II-b, BA-III, BA-III-a, etc.) has the structure of formula BA-III-c:



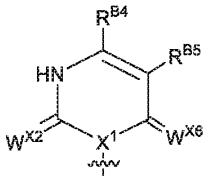
BA-III-c

[00290] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, BA-II-b, BA-III, BA-III-a, etc.) has the structure of formula BA-III-d:



BA-III-d

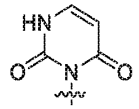
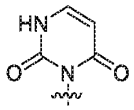
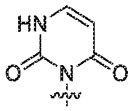
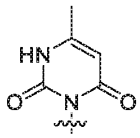
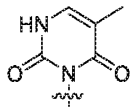
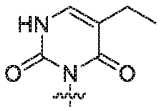
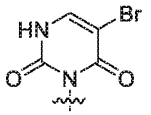
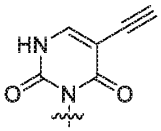
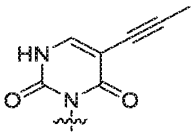
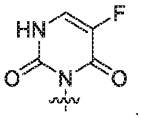
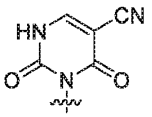
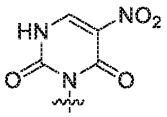
[00291] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-II, BA-II-a, BA-II-b, BA-III, BA-III-a, etc.) has the structure of formula BA-III-e:



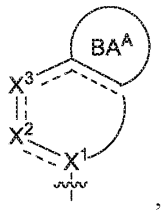
BA-III-e

In some embodiments, X^1 is N, and each of R^{B4} and R^{B5} is independently halogen or optionally substituted C_{1-10} alkyl. In some embodiments, each of R^{B4} and R^{B5} is independently halogen or optionally substituted C_{1-6} alkyl. In some embodiments, each of R^{B4} and R^{B5} is independently halogen or C_{1-6} alkyl. In some embodiments, each of R^{B4} and R^{B5} is independently halogen or C_{1-4} alkyl. In some embodiments, R^{B4} is –H. In some embodiments, R^{B4} is not –H. In some embodiments, R^{B4} is halogen. In some embodiments, R^{B4} is –F. In some embodiments, R^{B4} is –Cl. In some embodiments, R^{B4} is –Br. In some embodiments, R^{B4} is –CN. In some embodiments, R^{B4} is $-NO_2$. In some embodiments, R^{B4} is optionally substituted C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic. In some embodiments, R^{B4} is optionally substituted C_{1-4} aliphatic. In some embodiments, R^{B4} is optionally substituted C_{1-3} aliphatic. In some embodiments, R^{B4} is

optionally substituted C_{1-2} aliphatic. In some embodiments, R^{B4} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic optionally substituted halogen. In some embodiments, R^{B4} is C_{1-4} aliphatic optionally substituted halogen. In some embodiments, R^{B4} is C_{1-3} aliphatic optionally substituted halogen. In some embodiments, R^{B4} is C_{1-2} aliphatic optionally substituted halogen. In some embodiments, R^{B4} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic. In some embodiments, R^{B4} is C_{1-4} aliphatic. In some embodiments, R^{B4} is C_{1-3} aliphatic. In some embodiments, R^{B4} is C_{1-2} aliphatic. In some embodiments, R^{B4} is optionally substituted C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl. In some embodiments, R^{B4} is optionally substituted C_{1-4} alkyl. In some embodiments, R^{B4} is optionally substituted C_{1-3} alkyl. In some embodiments, R^{B4} is optionally substituted C_{1-2} alkyl. In some embodiments, R^{B4} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl optionally substituted with halogen. In some embodiments, R^{B4} is C_{1-4} alkyl optionally substituted with halogen. In some embodiments, R^{B4} is C_{1-3} alkyl optionally substituted with halogen. In some embodiments, R^{B4} is C_{1-2} alkyl optionally substituted with halogen. In some embodiments, R^{B4} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl. In some embodiments, R^{B4} is C_{1-4} alkyl. In some embodiments, R^{B4} is C_{1-4} alkyl. In some embodiments, R^{B4} is C_{1-3} alkyl. In some embodiments, R^{B4} is C_{1-2} alkyl. In some embodiments, R^{B4} is methyl. In some embodiments, R^{B4} is ethyl. In some embodiments, R^{B5} is –H. In some embodiments, R^{B5} is not –H. In some embodiments, R^{B5} is halogen. In some embodiments, R^{B5} is –F. In some embodiments, R^{B5} is –Cl. In some embodiments, R^{B5} is –Br. In some embodiments, R^{B5} is –CN. In some embodiments, R^{B5} is $-NO_2$. In some embodiments, R^{B5} is optionally substituted C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic. In some embodiments, R^{B5} is optionally substituted C_{1-4} aliphatic. In some embodiments, R^{B5} is optionally substituted C_{1-3} aliphatic. In some embodiments, R^{B5} is optionally substituted C_{1-2} aliphatic. In some embodiments, R^{B5} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic optionally substituted halogen. In some embodiments, R^{B5} is C_{1-4} aliphatic optionally substituted halogen. In some embodiments, R^{B5} is C_{1-3} aliphatic optionally substituted halogen. In some embodiments, R^{B5} is C_{1-2} aliphatic optionally substituted halogen. In some embodiments, R^{B5} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) aliphatic. In some embodiments, R^{B5} is C_{1-4} aliphatic. In some embodiments, R^{B5} is C_{1-3} aliphatic. In some embodiments, R^{B5} is C_{1-2} aliphatic. In some embodiments, R^{B5} is optionally substituted C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl. In some embodiments, R^{B5} is optionally substituted C_{1-4} alkyl. In some embodiments, R^{B5} is optionally substituted C_{1-3} alkyl. In some embodiments, R^{B5} is optionally substituted C_{1-2} alkyl. In some embodiments, R^{B5} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl optionally substituted with halogen. In some embodiments, R^{B5} is C_{1-4} alkyl optionally substituted with halogen. In some embodiments, R^{B5} is C_{1-3} alkyl optionally substituted with halogen. In some embodiments, R^{B5} is C_{1-2} alkyl optionally substituted with halogen. In some embodiments, R^{B5} is C_{1-6} (e.g., C_{1-5}, C_{1-4}, C_{1-3}, C_{1-2}, C_1, C_2, C_3, C_4, C_5, C_6, etc.) alkyl. In some embodiments, R^{B5} is C_{1-4} alkyl. In some embodiments, R^{B5} is C_{1-4} alkyl. In some embodiments, R^{B5} is C_{1-3} alkyl. In some embodiments, R^{B5} is C_{1-2} alkyl. In some embodiments, R^{B5} is methyl. In some embodiments, R^{B5} is ethyl. In some embodiments, R^{B5} is $-C\equiv CH$. In some embodiments, R^{B5} is $-C\equiv CHCH_3$. In some embodiments, W^{X2} and W^{X6} are each O.

In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is .In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is .

[00292] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-II, etc.) has the structure of formula BA-IV:

,

BA-IV

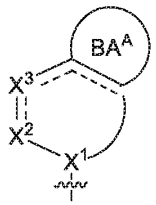
wherein:

Ring BA^A is an optionally substituted 5-14 membered, monocyclic, bicyclic or polycyclic ring having 0-5 heteroatoms, and

each other variable is independently as described herein.

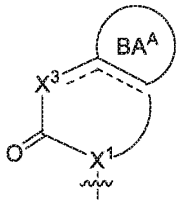
[00293] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-II, BA-II-a, etc.) has the

structure of formula BA-IV-a:



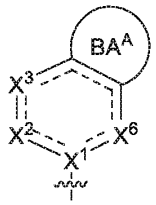
BA-IV-a

[00294] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-II, BA-II-a, etc.) has the structure of formula BA-IV-b:



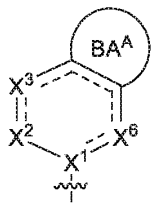
BA-IV-b

[00295] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-II, BA-III, BA-IV, etc.) has the structure of formula BA-V:



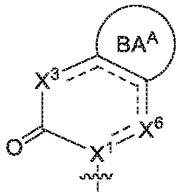
BA-V

[00296] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-II, BA-II-a, BA-III, BA-III-a, BA-IV, BA-IV-a, BA-V, etc.) has the structure of formula BA-V-a:



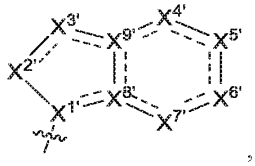
BA-V-a

[00297] In some embodiments, Ring BA (e.g., one of formula BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, etc.) has the structure of formula BA-V-a:



BA-V-b

[00298] In some embodiments, Ring BA has the structure of formula BA-VI:



BA-VI

wherein:

each ≡≡≡ is independent a single or double bond;

$X^{1'}$ is –N(–)– or –C(–)=;

$X^{2'}$ is $-C(W^{X2'})-$, $-C(R^{B2'})=$, $-C(OR^{B2'})=$, –N=, or optionally substituted –CH= or $-CH_2-$, wherein $R^{B2'}$ is halogen, –CN, $-NO_2$, or $-L^{B2'}-R'$, and $W^{X2'}$ is O, S or Se;

$X^{3'}$ is $-N(R^{B3'})-$, –N=, $-C(R^{B3'})=$ or optionally substituted –NH– or –CH=, wherein $R^{B3'}$ is halogen, –CN, $-NO_2$, or $-L^{B3'}-R'$;

$X^{4'}$ is $-C(R^{B4'})=$, $-C(OR^{B4'})=$, $-C(-N(R^{B4'})_2)=$, $-C(R^{B4'})_2-$, $-C(W^{X4'})-$, $-C(=NR^{B4'})-$, $-N(R^{B4'})-$, –N=, or optionally substituted –CH=, –NH– or $-CH_2-$, wherein each $R^{B4'}$ is independently halogen, –CN, $-NO_2$, or $-L^{B4'}-R^{B41'}$, or two $R^{B4'}$ on the same atom are taken together to form =O, $=C(-L^{B4'}-R^{B41'})_2$, $=N-L^{B4'}-R^{B41'}$, or optionally substituted $=CH_2$ or =NH, wherein each $R^{B41'}$ is independently –R', and $W^{X4'}$ is O, S or Se;

$X^{5'}$ is $-C(R^{B5'})_2-$, $-N(R^{B5'})-$, $-C(R^{B5'})=$, $-C(W^{X5'})-$, –N=, or optionally substituted –NH–, $-CH_2-$, or –CH=, wherein each $R^{B5'}$ is independently halogen, –CN, $-NO_2$, or $-L^{B5'}-R^{B51'}$, wherein $R^{B51'}$ is –R', $-N(R')_2$, –OR', or –SR', and $W^{X5'}$ is O, S, or Se;

$X^{6'}$ is $-C(R^{B6'})=$, $-C(OR^{B6'})=$, $-C(R^{B6'})_2-$, $-C(W^{X6'})-$, $-C(-N(R^{B6'})_2)=$, –N= or optionally substituted –NH–, $-CH_2-$ or –CH=, wherein each $R^{B6'}$ is independently halogen, –CN, $-NO_2$, or $-L^{B6'}-R^{B61'}$, or two $R^{B6'}$ on the same atom are taken together to form =O, $=C(-L^{B6'}-R^{B61'})_2$, $=N-L^{B6'}-R^{B61'}$, or optionally substituted $=CH_2$ or =NH, wherein each $R^{B61'}$ is independently R', and $W^{X6'}$ is O, S or Se;

$X^{7'}$ is $-C(R^{B7'})=$, $-C(OR^{B7'})=$, $-C(R^{B7'})_2-$, $-C(W^{X7'})-$, $-C(-N(R^{B7'})_2)=$, $-N(R^{B7'})-$, –N= or optionally substituted –NH–, $-CH_2-$ or –CH=, wherein each $R^{B7'}$ is independently halogen, –CN, $-NO_2$, or $-L^{B7'}-R^{B71'}$, or two $R^{B7'}$ on the same atom are taken together to form =O, $=C(-L^{B7'}-R^{B71'})_2$, $=N-L^{B7'}-R^{B71'}$, or optionally substituted $=CH_2$ or =NH, wherein each $R^{B71'}$ is independently R', and wherein $W^{X7'}$ is O, S, or

Se;

each of $X^{8'}$ and $X^{9'}$ is independently C or N;

each of $L^{B2'}$, $L^{B3'}$, $L^{B4'}$, $L^{B5'}$, $L^{B6'}$ and $L^{B7'}$ is independently L^{B}; and

each other variable is independently as described herein.

[00299] In some embodiments, ≡ is a single bond. In some embodiments, ≡ is a double bond.

[00300] In some embodiments, X^1 is –(N–)–. In some embodiments, X^1 is –C(–)=.

[00301] In some embodiments, W^{X2} is O. In some embodiments, W^{X2} is S. In some embodiments, W^{X2} is Se. In some embodiments, X^2 is –C(O)–. In some embodiments, X^2 is –C(S)–. In some embodiments, X^2 is –C(Se)–. In some embodiments, X^2 is $-C(R^{B2})=$. In some embodiments, X^2 is $-C(OR^{B2})=$. In some embodiments, X^2 is $-C(OR^{B2})=$, wherein R^{B2} is $-L^{B2}-R'$. In some embodiments, X^2 is optionally substituted –CH=. In some embodiments, X^2 is –CH=. In some embodiments, X^2 is $-C(R^{B2})=$, wherein R^{B2} is halogen, –CN, $-NO_2$, or $-L^{B2}-R'$. In some embodiments, X^2 is $-C(OR^{B2})=$, wherein R^{B2} is $-L^{B2}-R'$. In some embodiments, X^2 is –N=.

[00302] In some embodiments, L^{B2} is a covalent bond.

[00303] In some embodiments, R^{B2} is a protecting group, e.g., a hydroxyl protecting group suitable for oligonucleotide synthesis. In some embodiments, R^{B2} is R'. In some embodiments, R^{B2} is –H. In some embodiments, R^{B2} is halogen. In some embodiments, R^{B2} is –F. In some embodiments, R^{B2} is –Cl. In some embodiments, R^{B2} is –Br. In some embodiments, R^{B2} is –I. In some embodiments, R^{B2} is –CN. In some embodiments, R^{B2} is $-NO_2$. In some embodiments, R^{B2} is $-L^{B2}-R'$.

[00304] In some embodiments, X^3 is $-C(R^{B2})=$. In some embodiments, X^3 is optionally substituted –CH=. In some embodiments, X^3 is –CH=. In some embodiments, X^3 is $-N(R^{B3})-$. In some embodiments, X^3 is $-N(R^{B3})-$, wherein R^{B3} is $-L^{B3}-R'$. In some embodiments, X^3 is $-N(R^{B3})-$ wherein R^{B3} is $-L^{B3}-R'$. In some embodiments, X^3 is optionally substituted –NH–. In some embodiments, X^3 is –NH–. In some embodiments, X^3 is –N=.

[00305] In some embodiments, L^{B3} is a covalent bond.

[00306] In some embodiments, R^{B3} is a protecting group, e.g., an amino protecting group suitable for oligonucleotide synthesis (e.g., Bz). In some embodiments, R^{B3} is R'. In some embodiments, R^{B3} is –C(O)R. In some embodiments, R^{B3} is R. In some embodiments, R^{B3} is –H. In some embodiments, R^{B3} is halogen. In some embodiments, R^{B3} is –F. In some embodiments, R^{B3} is –Cl. In some embodiments, R^{B3} is –Br. In some embodiments, R^{B3} is –I. In some embodiments, R^{B3} is –CN. In some embodiments, R^{B3} is $-NO_2$. In some embodiments, R^{B3} is $-L^{B3}-R'$.

[00307] In some embodiments, X^4 is $-C(R^{B4})=$. In some embodiments, X^4 is –C(R)=. In some embodiments, X^4 is –CH=. In some embodiments, X^4 is –CH=. In some embodiments, X^4 is $-C(OR^{B4})=$. In some embodiments, X^4 is $-C(-N(R^{B4})_2)=$. In some embodiments, X^4 is $-C(-N(R^{B4})_2)=$, wherien each R^{B4} is independently $-L^{B4}-R^{B41}$. In some embodiments, X^4 is $-C(-NHR^{B4})=$. In some embodiments, X^4 is $-C(-NHR')=$. In some embodiments, X^4 is $-C(-NHR')=$. In some embodiments, X^4 is optionally substituted

–C(–NH_2)=. In some embodiments, X^4 is –C(–NH_2)=. In some embodiments, X^4 is –C(–NHC(O)R)=. In some embodiments, X^4 is –C(R^{B4})$_2$–. In some embodiments, X^4 is optionally substituted –CH_2–. In some embodiments, X^4 is –CH_2–. In some embodiments, X^4 is –C(O)–. In some embodiments, X^4 is –C(S)–. In some embodiments, X^4 is –C(Se)–. In some embodiments, X^4 is –C(O)–, wherein O forms a intramolecular hydrogen bond. In some embodiments, O forms a hydrogen bond with a hydrogen bond donor of X^5 of the same BA. In some embodiments, X^4 is –C(=NR^{B4})–. In some embodiments, X^4 is –C((=NR^{B4})–, wherein N forms a intramolecular hydrogen bond. In some embodiments, N forms a hydrogen bond with a hydrogen bond donor of X^5 of the same BA.

[00308] In some embodiments, R^{B4} is –L^{B4}–R^{B41}. In some embodiments, two R^{B4} on the same atom are taken together to form =O, =C(–L^{B4}–R^{B41})$_2$, =N–L^{B4}– R^{B41}, or optionally substituted =CH_2 or =NH.

[00309] In some embodiments, two R^{B4} on the same atom are taken together to form =O. In some embodiments, two R^{B4} on the same atom are taken together to form =C(–L^{B4}–R^{B41})$_2$. In some embodiments, =C(–L^{B4}–R^{B41})$_2$ is =CH–L^{B4}–R^{B41}. In some embodiments, =C(–L^{B4}–R^{B41})$_2$ is =CHR'. In some embodiments, =C(–L^{B4}–R^{B41})$_2$ is =CHR. In some embodiments, two R^{B4} on the same atom are taken together to form =N–L^{B4}– R^{B41}. In some embodiments, =N–L^{B4}– R^{B41} is =N–R. In some embodiments, two R^{B4} on the same atom are taken together to form =CH_2. In some embodiments, two R^{B4} on the same atom are taken together to form =NH. In some embodiments, a formed group is a suitable protecting group, e.g., amino protecting group, for oligonucleotide synthesis.

[00310] In some embodiments, X^4 is –C(–N=C(–L^{B4}–R^{B41})$_2$)=. In some embodiments, X^4 is –C(–N=CH–L^{B4}–R^{B41})=. In some embodiments, X^4 is –C(–N=CH–N(CH_3)$_2$)=.

[00311] In some embodiments, R of X^4 (e.g., of –C(=N–R)–, =C(R)–, etc.) are optionally taken together with another R, e.g., of X^5, to form a ring as described herein.

[00312] In some embodiments, R^{B4} is R'. In some embodiments, R^{B4} is R. In some embodiments, R^{B4} is –H. In some embodiments, R^{B4} is halogen. In some embodiments, R^{B4} is –F. In some embodiments, R^{B4} is –Cl. In some embodiments, R^{B4} is –Br. In some embodiments, R^{B4} is –I. In some embodiments, R^{B4} is –CN. In some embodiments, R^{B4} is –NO_2. In some embodiments, R^{B4} is –L^{B4}–R'. In some embodiments, R^{B4} is a protecting group, e.g., an amino or hydroxyl protecting group suitable for oligonucleotide synthesis. In some embodiments, R^{B4} is R'. In some embodiments, R^{B4} is –CH_2CH_2–(4-nitrophenyl).

[00313] In some embodiments, L^{B4} is a covalent bond. In some embodiments, L^{B4} is not a covalent bond. In some embodiments, at least one methylene unit is replaced with –C(O)–. In some embodiments, at least one methylene unit is replaced with –C(O)N(R')–. In some embodiments, at least one methylene unit is replaced with –N(R')–. In some embodiments, at least one methylene unit is replaced with –NH–. In some embodiments, L^{B4} is or comprises optionally substituted –N=CH–.

[00314] In some embodiments, R^{B41} is R'. In some embodiments, R^{B41} is –H. In some embodiments, R^{B41} is R. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl.

[00315] In some embodiments, X^5 is –C(R^{B5})$_2$–. In some embodiments, X^5 is –CHR^{B5}–. In some

embodiments, X^5 is optionally substituted $-CH_2-$. In some embodiments, X^5 is $-CH_2-$. In some embodiments, X^5 is $-N(R^{B5})-$. In some embodiments, X^5 is optionally substituted $-NH-$. In some embodiments, X^5 is $-NH-$. In some embodiments, X^5 is $-C(R^{B5})=$. In some embodiments, X^5 is $-C(R)=$. In some embodiments, X^5 is optionally substituted $-CH=$. In some embodiments, X^5 is $-CH=$. In some embodiments, X^5 is $-N=$. In some embodiments, X^5 is $-C(O)-$. In some embodiments, X^5 is $-C(S)-$. In some embodiments, X^5 is $-C(Se)-$.

[00316] In some embodiments, R^{B5} is halogen. In some embodiments, R^{B5} is $-L^{B5}-R^{B51}$. In some embodiments, R^{B5} is $-L^{B5}-R^{B51}$, wherein R^{B51} is R', $-NHR'$, $-OH$, or $-SH$. In some embodiments, R^{B5} is $-L^{B5}-R^{B51}$, wherein R^{B51} is $-NHR$, $-OH$, or $-SH$. In some embodiments, R^{B5} is $-L^{B5}-R^{B51}$, wherein R^{B51} is $-NH_2$, $-OH$, or $-SH$. In some embodiments, R^{B5} is $-C(O)-R^{B51}$. In some embodiments, R^{B5} is R'. In some embodiments, R^{B5} is R. In some embodiments, R^{B5} is $-H$. In some embodiments, R^{B5} is $-OH$. In some embodiments, R^{B5} is $-CH_2OH$. In some embodiments, R^{B5} is halogen. In some embodiments, R^{B5} is $-F$. In some embodiments, R^{B5} is $-Cl$. In some embodiments, R^{B5} is $-Br$. In some embodiments, R^{B5} is $-I$. In some embodiments, R^{B5} is $-CN$. In some embodiments, R^{B5} is $-NO_2$. In some embodiments, R^{B5} is $-L^{B5}-R'$.

[00317] In some embodiments, when X^4 is $-C(O)-$, X^5 is $-C(R^{B5})_2-$, $-C(R^{B5})=$, or $-N(R^{B5})-$, wherein R^{B5} is $-L^{B5}-R^{B51}$, wherein R^{B51} is $-NHR'$, $-OH$, or $-SH$. In some embodiments, X^4 is $-C(O)-$, and R^{B51} is or comprises a hydrogen bond donor, which forms a hydrogen bond with the O of X^4.

[00318] In some embodiments, L^{B5} is a covalent bond. In some embodiments, L^{B5} is or comprises $-C(O)-$. In some embodiments, L^{B5} is or comprises $-O-$. In some embodiments, L^{B5} is or comprises $-OC(O)-$. In some embodiments, L^{B5} is or comprises $-CH_2OC(O)-$.

[00319] In some embodiments, R^{51} is $-R'$. In some embodiments, R^{51} is $-R$. In some embodiments, R^{51} is $-H$. In some embodiments, R^{51} is $-N(R')_2$. In some embodiments, R^{51} is $-NHR'$. In some embodiments, R^{51} is $-NHR$. In some embodiments, R^{51} is $-NH_2$. In some embodiments, R^{51} is $-OR'$. In some embodiments, R^{51} is $-OR$. In some embodiments, R^{51} is $-OH$. In some embodiments, R^{51} is $-SR'$. In some embodiments, R^{51} is $-SR$. In some embodiments, R^{51} is $-SH$. In some embodiments, R is benzyl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl. In some embodiments, R is methyl.

[00320] In some embodiments, R^{B5} is $-C(O)-R^{B51}$. In some embodiments, R^{B5} is $-C(O)NHCH_2Ph$. In some embodiments, R^{B5} is $-C(O)NHPh$. In some embodiments, R^{B5} is $-C(O)NHCH_3$. In some embodiments, R^{B5} is $-OC(O)-R^{B51}$. In some embodiments, R^{B5} is $-OC(O)-R$. In some embodiments, R^{B5} is $-OC(O)CH_3$.

[00321] In some embodiments, X^5 is directly bonded to X^1, and Ring BA is 5-membered.

[00322] In some embodiments, X^6 is $-C(R^{B6})=$. In some embodiments, X^6 is optionally substituted $-CH=$. In some embodiments, X^6 is $-CH=$. In some embodiments, X^6 is $-C(OR^{B6})=$. In some embodiments, X^6 is $-C(R^{B6})_2-$. In some embodiments, X^6 is optionally substituted $-CH_2-$. In some embodiments, X^6 is $-CH_2-$. In some embodiments, X^6 is $-C(O)-$. In some embodiments, X^6 is $-C(S)-$. In some embodiments, X^6 is $-C(Se)-$. In some embodiments, X^6 is $-N=$.

[00323] In some embodiments, R^{B6} is $-L^{B6}-R^{B61}$. In some embodiments, two R^{B6} on the same atom are taken together to form =O, $=C(-L^{B6}-R^{B61})_2$, $=N-L^{B6}-R^{B61}$, or optionally substituted $=CH_2$ or =NH. In some

embodiments, two R^{B6} on the same atom are taken together to form =O. In some embodiments, L^{B6} is a covalent bond. In some embodiments, R^{B6} is R. In some embodiments, R^{B6} is –H.

[00324] In some embodiments, R^{B6} is a protecting group, e.g., an amino or hydroxyl protecting group suitable for oligonucleotide synthesis. In some embodiments, R^{B6} is R. In some embodiments, R^{B6} is –H. In some embodiments, R^{B6} is halogen. In some embodiments, R^{B6} is –F. In some embodiments, R^{B6} is –Cl. In some embodiments, R^{B6} is –Br. In some embodiments, R^{B6} is –I. In some embodiments, R^{B6} is –CN. In some embodiments, R^{B6} is $-NO_2$. In some embodiments, R^{B6} is $-L^{B6}-R'$.

[00325] In some embodiments, L^{B6} is a covalent bond. In some embodiments, L^{B6} is optionally substituted C_{1-10} alkylene. In some embodiments, L^{B6} is $-CH_2CH_2-$. In some embodiments, R^{B6} is $-CH_2CH_2-$(4-nitrophenyl).

[00326] In some embodiments, R^{B61} is R'. In some embodiments, R^{B61} is R. In some embodiments, R^{B61} is –H.

[00327] In some embodiments, Ring BA^A is monocyclic. In some embodiments, Ring BA^A is 5-membered. In some embodiments, Ring BA^A is 6-membered. In some embodiments, Ring BA^A is bicyclic. In some embodiments, Ring BA^A is 9-membered. In some embodiments, Ring BA^A is 10-membered. In some embodiments, Ring BA^A has one heteroatom. In some embodiments, Ring BA^A has 2 heteroatoms. In some embodiments, Ring BA^A has 3 heteroatoms. In some embodiments, Ring BA^A has 4 heteroatoms. In some embodiments, Ring BA^A has 5 heteroatoms. In some embodiments, a heteroatom is nitrogen. In some embodiments, a heteroatom is oxygen.

[00328] In some embodiments, $X^{1'}$ is –(N–)–. In some embodiments, $X^{1'}$ is –C(–)=.

[00329] In some embodiments, $X^{2'}$ is –C(O)–. In some embodiments, $X^{2'}$ is –C(S)–. In some embodiments, $X^{2'}$ is –C(Se)–. In some embodiments, $X^{2'}$ is $-C(R^{B2'})=$. In some embodiments, $X^{2'}$ is optionally substituted $-CH_2-$. In some embodiments, $X^{2'}$ is $-CH_2-$. In some embodiments, $X^{2'}$ is optionally substituted –CH=. In some embodiments, $X^{2'}$ is –CH=. In some embodiments, $X^{2'}$ is $-C(OR^{B2'})=$. In some embodiments, $X^{2'}$ is $-C(OR^{B2'})=$, wherein $R^{B2'}$ is $-L^{B2'}-R'$. In some embodiments, $X^{2'}$ is –N=.

[00330] In some embodiments, $L^{B2'}$ is a covalent bond.

[00331] In some embodiments, $R^{B2'}$ is R'. In some embodiments, $R^{B2'}$ is R. In some embodiments, $R^{B2'}$ is not –H. In some embodiments, $R^{B2'}$ is –H. In some embodiments, $R^{B2'}$ is halogen. In some embodiments, $R^{B2'}$ is –F. In some embodiments, $R^{B2'}$ is –Cl. In some embodiments, $R^{B2'}$ is –Br. In some embodiments, $R^{B2'}$ is –I. In some embodiments, $R^{B2'}$ is –CN. In some embodiments, $R^{B2'}$ is $-NO_2$. In some embodiments, $R^{B2'}$ is $-L^{B2'}-R'$.

[00332] In some embodiments, $X^{3'}$ is $-N(R^{B3'})-$. In some embodiments, $X^{3'}$ is $-N(R^{B3'})-$, wherein $R^{B3'}$ is $-L^{B3'}-R'$. In some embodiments, $X^{3'}$ is –N(R')–. In some embodiments, $X^{3'}$ is optionally substituted –NH–. In some embodiments, $X^{3'}$ is –NH–. In some embodiments, $X^{3'}$ is –N=. In some embodiments, $X^{3'}$ is $-C(R^{B3'})=$.

[00333] In some embodiments, $L^{B3'}$ is a covalent bond.

[00334] In some embodiments, $R^{B3'}$ is R'. In some embodiments, $R^{B3'}$ is R. In some embodiments, $R^{B3'}$ is −H. In some embodiments, $R^{B3'}$ is not −H. In some embodiments, $R^{B3'}$ is halogen. In some embodiments, $R^{B3'}$ is −F. In some embodiments, $R^{B3'}$ is −Cl. In some embodiments, $R^{B3'}$ is −Br. In some embodiments, $R^{B3'}$ is −I. In some embodiments, $R^{B3'}$ is −CN. In some embodiments, $R^{B3'}$ is $-NO_2$. In some embodiments, $R^{B3'}$ is $-L^{B3'}-R'$.

[00335] In some embodiments, $X^{4'}$ is $-C(R^{B4'})=$. In some embodiments, $X^{4'}$ is optionally substituted −CH=. In some embodiments, $X^{4'}$ is −CH=. In some embodiments, $X^{4'}$ is $-C(OR^{B4'})=$. In some embodiments, $X^{4'}$ is $-C(OR^{B4'})=$, wherein $R^{B4'}$ is $-L^{B4'}- R^{B41'}$. In some embodiments, $X^{4'}$ is $-C(-N(R^{B4'})_2)=$. In some embodiments, $X^{4'}$ is $-C(-NHR^{B4'})=$. In some embodiments, $X^{4'}$ is optionally substituted $-C(-NH_2)=$. In some embodiments, $X^{4'}$ is $-C(-NH_2)=$. In some embodiments, $X^{4'}$ is $-C(-NHR')=$. In some embodiments, $X^{4'}$ is $-C(-N(R')_2)=$. In some embodiments, $X^{4'}$ is $-C(-NHC(O)R')=$. In some embodiments, $X^{4'}$ is $-C(-NHC(O)NHR')=$. In some embodiments, $X^{4'}$ is $-C(-NHC(O)N(R')_2)=$. In some embodiments, $X^{4'}$ is $-C(-N(R')C(O)N(R')_2)=$. In some embodiments, R' is −H. In some embodiments, R' is optionally substituted C_{1-6} aliphatic. In some embodiments, R' is optionally substituted C_{1-6} alkyl. In some embodiments, R' is C_{1-6} alkyl. In some embodiments, R' is methyl. In some embodiments, R' is ethyl. In some embodiments, R' is isopropyl. In some embodiments, R' is optionally substituted phenyl. In some embodiments, R' is phenyl. In some embodiments, R' is optionally substituted naphthyl. In some embodiments, R' is optionally substituted 2-naphthyl. In some embodiments, R' is 2-naphthyl. In some embodiments, R' is C_{1-6} alkyl. In some embodiments, $X^{4'}$ is $-C(-NH_2)=$. In some embodiments, $X^{4'}$ is $-C(-N(CH_3)_2)=$. In some embodiments, $X^{4'}$ is −C(−NHEt)=. In some embodiments, $X^{4'}$ is −C(−NH(i-Pr))=. In some embodiments, $X^{4'}$ is −C(−NHC(O)Ph)=. In some embodiments, $X^{4'}$ is $-C(-NHC(O)NHCH_3)=$. In some embodiments, $X^{4'}$ is −C(−NHC(O)NHPh)=. In some embodiments, $X^{4'}$ is −C(−NHC(O)NH(2-naphthyl))=. In some embodiments, $X^{4'}$ is $-C(R^{B4'})_2-$. In some embodiments, $X^{4'}$ is optionally substituted $-CH_2-$. In some embodiments, $X^{4'}$ is $-CH_2-$. In some embodiments, $X^{4'}$ is −C(O)−. In some embodiments, $X^{4'}$ is −C(S)−. In some embodiments, $X^{4'}$ is −C(Se)−. In some embodiments, $X^{4'}$ is $-C(=NR^{B4'})-$. In some embodiments, $X^{4'}$ is $-N(R^{B4'})-$. In some embodiments, $X^{4'}$ is optionally substituted −NH−. In some embodiments, $X^{4'}$ is −NH−. In some embodiments, $X^{4'}$ is −N=.

[00336] In some embodiments, $R^{B4'}$ is $-L^{B4'}-R^{B41'}$. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form =O, $=C(-L^{B4'}-R^{B41'})_2$, $=N-L^{B4'}- R^{B41'}$, or optionally substituted $=CH_2$ or =NH. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form =O. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form $=C(-L^{B4'}-R^{B41'})_2$. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form $=N-L^{B4'}- R^{B41'}$. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form $=CH_2$. In some embodiments, two $R^{B4'}$ on the same atom are taken together to form =NH. In some embodiments, a formed group is a suitable protecting group, e.g., amino protecting group, for oligonucleotide synthesis.

[00337] In some embodiments, $X^{4'}$ is $-C(-N=C(-L^{B4'}-R^{B41'})_2)=$. In some embodiments, $X^{4'}$ is

$-C(-N=CH-L^{B4'}-R^{B41'})=$. In some embodiments, $X^{4'}$ is $-C(-N=CH-N(CH_3)_2)=$.

[00338] In some embodiments, $R^{B4'}$ is R'. In some embodiments, $R^{B4'}$ is R. In some embodiments, $R^{B4'}$ is −H. In some embodiments, $R^{B4'}$ is not −H. In some embodiments, $R^{B4'}$ is halogen. In some embodiments, $R^{B4'}$ is −F. In some embodiments, $R^{B4'}$ is −Cl. In some embodiments, $R^{B4'}$ is −Br. In some embodiments, $R^{B4'}$ is −I. In some embodiments, $R^{B4'}$ is −CN. In some embodiments, $R^{B4'}$ is $-NO_2$. In some embodiments, $R^{B4'}$ is $-L^{B4'}-R'$.

[00339] In some embodiments, $R^{B4'}$ is a protecting group, e.g., an amino or hydroxyl protecting group suitable for oligonucleotide synthesis. In some embodiments, $R^{B4'}$ is R'. In some embodiments, $R^{B4'}$ is $-CH_2CH_2-$(4-nitrophenyl).

[00340] In some embodiments, $L^{B4'}$ is a covalent bond. In some embodiments, $L^{B4'}$ is optionally substituted C_{1-10} alkylene. In some embodiments, $L^{B4'}$ is $-CH_2CH_2-$. In some embodiments, at least one methylene unit is replaced with $-N(R')-$. In some embodiments, R' is R. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl. In some embodiments, R is methyl. In some embodiments, R is −H.

[00341] In some embodiments, $R^{B41'}$ is R'. In some embodiments, $R^{B41'}$ is R. In some embodiments, $R^{B41'}$ is −H.

[00342] In some embodiments, $X^{5'}$ is $-C(R^{B5'})_2-$. In some embodiments, $X^{5'}$ is optionally substituted $-CH_2-$. In some embodiments, $X^{5'}$ is $-CH_2-$. In some embodiments, $X^{5'}$ is $-N(R^{B5'})-$. In some embodiments, $X^{5'}$ is optionally substituted −NH−. In some embodiments, $X^{5'}$ is −NH−. In some embodiments, $X^{5'}$ is $-C(R^{B5'})=$. In some embodiments, $X^{5'}$ is optionally substituted −CH=. In some embodiments, $X^{5'}$ is −CH=. In some embodiments, $X^{5'}$ is $-C(O)-$. In some embodiments, $X^{5'}$ is $-C(S)-$. In some embodiments, $X^{5'}$ is $-C(Se)-$. In some embodiments, $X^{5'}$ is −N=.

[00343] In some embodiments, $L^{B5'}$ is a covalent bond.

[00344] In some embodiments, $R^{B5'}$ is R'. In some embodiments, $R^{B5'}$ is R. In some embodiments, $R^{B5'}$ is −H. In some embodiments, $R^{B5'}$ is not −H.

[00345] In some embodiments, $R^{B5'}$ is halogen. In some embodiments, $R^{B5'}$ is −F. In some embodiments, $R^{B5'}$ is −Cl. In some embodiments, $R^{B5'}$ is −Br. In some embodiments, $R^{B5'}$ is −I. In some embodiments, $R^{B5'}$ is −CN. In some embodiments, $R^{B5'}$ is $-NO_2$. In some embodiments, $R^{B5'}$ is $-L^{B5'}-R'$.

[00346] In some embodiments, $X^{6'}$ is $-C(R^{B6'})=$. In some embodiments, $X^{6'}$ is optionally substituted −CH=. In some embodiments, $X^{6'}$ is −CH=. In some embodiments, $X^{6'}$ is $-C(OR^{B6'})=$. In some embodiments, $X^{6'}$ is $-C(OR^{B6'})=$, wherein $R^{B6'}$ is $-L^{B6'}-R^{B61'}$. In some embodiments, $X^{6'}$ is $-C(R^{B6'})_2-$. In some embodiments, $X^{6'}$ is optionally substituted $-CH_2-$. In some embodiments, $X^{6'}$ is $-CH_2-$. In some embodiments, $X^{6'}$ is $-C(O)-$. In some embodiments, $X^{6'}$ is $-C(S)-$. In some embodiments, $X^{6'}$ is $-C(Se)-$. In some embodiments, $X^{6'}$ is $-C(-N(R^{B6'})_2)=$. In some embodiments, $X^{6'}$ is $-C(-N(R^{B6'})_2)=$, wherein each $R^{B6'}$ is independently $-L^{B6'}-R^{B61'}$. In some embodiments, $X^{6'}$ is $-C(-N(R')_2)=$. In some embodiments, $X^{6'}$ is $-C(-NHR')=$. In some embodiments, $X^{6'}$ is $-C(-NHC(O)R)=$. In some embodiments, $X^{6'}$ is −N=.

[00347] In some embodiments, $R^{B6'}$ is $-L^{B6'}-R^{B61'}$. In some embodiments, two $R^{B6'}$ on the same atom are taken together to form =O, $=C(-L^{B6'}-R^{B61'})_2$, $=N-L^{B6'}-R^{B61'}$, or optionally substituted $=CH_2$ or =NH. In some embodiments, two $R^{B6'}$ on the same atom are taken together to form =O.

[00348] In some embodiments, $L^{B6'}$ is a covalent bond. In some embodiments, $L^{B6'}$ is optionally substituted C_{1-10} alkylene. In some embodiments, $L^{B6'}$ is $-CH_2CH_2-$.

[00349] In some embodiments, $R^{B6'}$ is R'. In some embodiments, $R^{B6'}$ is R. In some embodiments, $R^{B6'}$ is –H. In some embodiments, $R^{B6'}$ is not –H. In some embodiments, $R^{B6'}$ is a protecting group, e.g., an amino or hydroxyl protecting group suitable for oligonucleotide synthesis. In some embodiments, $R^{B6'}$ is R'. In some embodiments, $R^{B6'}$ is $-CH_2CH_2-$(4-nitrophenyl).

[00350] In some embodiments, $R^{B61'}$ is R'. In some embodiments, $R^{B61'}$ is R. In some embodiments, $R^{B61'}$ is –H. In some embodiments, $R^{B61'}$ is not –H.

[00351] In some embodiments, $R^{B6'}$ is halogen. In some embodiments, $R^{B6'}$ is –F. In some embodiments, $R^{B6'}$ is –Cl. In some embodiments, $R^{B6'}$ is –Br. In some embodiments, $R^{B6'}$ is –I. In some embodiments, $R^{B6'}$ is –CN. In some embodiments, $R^{B6'}$ is $-NO_2$. In some embodiments, $R^{B6'}$ is $-L^{B6'}-R'$.

[00352] In some embodiments, $X^{7'}$ is $-C(R^{B7'})=$. In some embodiments, $X^{7'}$ is optionally substituted –CH=. In some embodiments, $X^{7'}$ is –CH=. In some embodiments, $X^{7'}$ is $-C(OR^{B7'})=$. In some embodiments, $X^{7'}$ is $-C(OR^{B7'})=$, wherein $R^{B7'}$ is $-L^{B7'}-R^{B71'}$. In some embodiments, $X^{7'}$ is $-C(R^{B7'})_2-$. In some embodiments, $X^{7'}$ is optionally substituted $-CH_2-$. In some embodiments, $X^{7'}$ is $-CH_2-$. In some embodiments, $X^{7'}$ is –C(O)–. In some embodiments, $X^{7'}$ is –C(S)–. In some embodiments, $X^{7'}$ is –C(Se)–. In some embodiments, $X^{7'}$ is $-C(-N(R^{B7'})_2)=$. In some embodiments, $X^{7'}$ is $-C(-N(R^{B7'})_2)=$, wherein each $R^{B7'}$ is independently $-L^{B7'}-R^{B71'}$. In some embodiments, $X^{7'}$ is $-N(R^{B7'})-$. In some embodiments, $X^{7'}$ is optionally substituted –NH–. In some embodiments, $X^{7'}$ is –NH–. In some embodiments, $X^{7'}$ is –N=.

[00353] In some embodiments, $R^{B7'}$ is $-L^{B7'}-R^{B71'}$. In some embodiments, two $R^{B7'}$ on the same atom are taken together to form =O, $=C(-L^{B7'}-R^{B71'})_2$, $=N-L^{B7'}-R^{B71'}$, or optionally substituted $=CH_2$ or =NH. In some embodiments, two $R^{B7'}$ on the same atom are taken together to form =O. In some embodiments, $L^{B7'}$ is a covalent bond. In some embodiments, $R^{B7'}$ is R. In some embodiments, $R^{B7'}$ is –H. In some embodiments, $R^{B7'}$ is not –H. In some embodiments, $R^{B7'}$ is halogen. In some embodiments, $R^{B7'}$ is –F. In some embodiments, $R^{B7'}$ is –Cl. In some embodiments, $R^{B7'}$ is –Br. In some embodiments, $R^{B7'}$ is –I. In some embodiments, $R^{B7'}$ is –CN. In some embodiments, $R^{B7'}$ is $-NO_2$. In some embodiments, $R^{B7'}$ is $-L^{B7'}-R'$.

[00354] In some embodiments, $L^{B7'}$ is a covalent bond. In some embodiments, $L^{B7'}$ is optionally substituted C_{1-10} alkylene. In some embodiments, $L^{B7'}$ is $-CH_2CH_2-$.

[00355] In some embodiments, $R^{B71'}$ is R'. In some embodiments, $R^{B71'}$ is R. In some embodiments, $R^{B71'}$ is –H. In some embodiments, $R^{B71'}$ is not –H.

[00356] In some embodiments, L^B is a covalent bond. In some embodiments, L^B is an optionally substituted bivalent C_{1-10} saturated or partially unsaturated aliphatic chain, wherein one or more methylene unit is optionally and independently replaced with –Cy–, –O–, –S–, –N(R')–, –C(O)–, –C(S)–, –C(NR')–,

−C(O)N(R')−, −N(R')C(O)N(R')−, −N(R')C(O)O−, −S(O)−, −$S(O)_2$−, −$S(O)_2$N(R')−, −C(O)S−, or −C(O)O−. In some embodiments, L^B is an optionally substituted bivalent C_{1-10} saturated or partially unsaturated heteroaliphatic chain having 1-6 heteroatoms, wherein one or more methylene unit is optionally and independently replaced with −Cy−, −O−, −S−, −N(R')−, −C(O)−, −C(S)−, −C(NR')−, −C(O)N(R')−, −N(R')C(O)N(R')−, −N(R')C(O)O−, −S(O)−, −$S(O)_2$−, −$S(O)_2$N(R')−, −C(O)S−, or −C(O)O−. In some embodiments, at least methylene unit is replaced. In some embodiments, L^B is optionally substituted C_{1-10} alkylene. In some embodiments, L^B is optionally substituted C_{1-6} alkylene. In some embodiments, L^B is optionally substituted C_{1-4} alkylene. In some embodiments, L^B is −CH_2CH_2−. In some embodiments, at least one methylene unit is replaced with −C(O)−. In some embodiments, at least one methylene unit is replaced with −C(O)N(R')−. In some embodiments, at least one methylene unit is replaced with −N(R')−. In some embodiments, at least one methylene unit is replaced with −NH−. In some embodiments, at least one methylene unit is replaced with −Cy−. In some embodiments, L^B is or comprises optionally substituted −N=CH−. In some embodiments, L^B is or comprises −C(O)−. In some embodiments, L^B is or comprises −O−. In some embodiments, L^B is or comprises −OC(O)−. In some embodiments, L^B is or comprises −CH_2OC(O)−.

[00357] In some embodiments, each −Cy− is independently an optionally substituted, 3-20 membered, monocyclic, bicyclic or polycyclic, saturated, partially saturated or aromatic ring having 0-10 heteroatoms. Suitable monocyclic unit(s) of −Cy− are described herein. In some embodiments, −Cy− is monocyclic. In some embodiments, −Cy− is bicyclic. In some embodiments, −Cy− is polycyclic. In some embodiments, −Cy− is an optionally substituted bivalent 3-10 membered monocyclic, saturated or partially unsaturated ring having 0-5 heteroatoms. In some embodiments, −Cy− is an optionally substituted bivalent 5-10 membered aromatic ring having 0-5 heteroatoms. In some embodiments, −Cy− is optionally substituted phenylene. In some embodiments, −Cy− is phenylene.

[00358] In some embodiments, R' is R. In some embodiments, R' is −C(O)R. In some embodiments, R' is −C(O)OR. In some embodiments, R' is −C(O)N$(R)_2$. In some embodiments, R' is −SO_2R.

[00359] In some embodiments, R' in various structures is a protecting group (e.g., for amino, hydroxyl, etc.), e.g., one suitable for oligonucleotide synthesis. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl. In some embodiments, R is 4-nitrophenyl. In some embodiments, R is −CH_2CH_2−(4-nitrophenyl). In some embodiments, R' is −C(O)NPh_2.

[00360] In some embodiments, each R is independently −H, or an optionally substituted group selected from C_{1-10} aliphatic, C_{1-10} heteroaliphatic having 1-5 heteroatoms, C_{6-14} aryl, C_{6-20} arylaliphatic, C_{6-20} arylheteroaliphatic having 1-5 heteroatoms, 5-14 membered heteroaryl having 1-5 heteroatoms, and 3-10 membered heterocyclyl having 1-5 heteroatoms, or

two R groups are optionally and independently taken together to form a covalent bond, or:

two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-15 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 (e.g., 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) heteroatoms; or:

two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-15 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 (e.g., 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) heteroatoms.

[00361] In some embodiments, each R is independently −H, or an optionally substituted group selected from C_{1-20} aliphatic, C_{1-20} heteroaliphatic having 1-10 heteroatoms, C_{6-30} aryl, C_{6-30} arylaliphatic, C_{6-30} arylheteroaliphatic having 1-10 heteroatoms, 5-20 membered heteroaryl having 1-10 heteroatoms, and 3-30 membered heterocyclyl having 1-10 heteroatoms. In some embodiments, each R is independently −H, or an optionally substituted group selected from C_{1-10} aliphatic, C_{1-10} heteroaliphatic having 1-5 heteroatoms, C_{6-14} aryl, C_{6-20} arylaliphatic, C_{6-20} arylheteroaliphatic having 1-5 heteroatoms, 5-14 membered heteroaryl having 1-5 heteroatoms, and 3-10 membered heterocyclyl having 1-5 heteroatoms. In some embodiments, two R groups are optionally and independently taken together to form a covalent bond. In some embodiments, two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-20 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms. In some embodiments, two groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-20 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms. In some embodiments, two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms. In some embodiments, two groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms. In some embodiments, a formed ring is monocyclic. In some embodiments, a formed ring is bicyclic. In some embodiments, a formed ring is polycyclic. In some embodiments, each monocyclic ring unit is independently 3-10 (e.g., 3-8, 3-7, 3-6, 5-10, 5-8, 5-7, 5-6, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) membered, and is independently saturated, partially saturated, or aromatic, and independently has 0-5 heteroatom. In some embodiments, a ring is saturated. In some embodiments, a ring is partially saturated. In some embodiments, a ring is aromatic. In some embodiments, a formed ring has 1-5 heteroatom. In some embodiments, a formed ring has 1 heteroatom. In some embodiments, a formed ring has 2 heteroatoms. In some embodiments, a heteroatom is nitrogen. In some embodiments, a heteroatom is oxygen.

[00362] In some embodiments, R is −H.

[00363] In some embodiments, R is optionally substituted C_{1-20}, C_{1-15}, C_{1-10}, C_{1-8}, C_{1-6}, C_{1-5}, C_{1-4}, C_{1-3}, or C_{1-2} aliphatic. In some embodiments, R is optionally substituted alkyl. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted methyl. In some embodiments, R is optionally substituted cycloaliphatic. In some embodiments, R is optionally substituted cycloalkyl.

[00364] In some embodiments, R is optionally substituted C_{1-20} heteroaliphatic having 1-10 heteroatoms.

[00365] In some embodiments, R is optionally substituted C_{6-20} aryl. In some embodiments, R is optionally

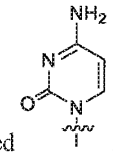
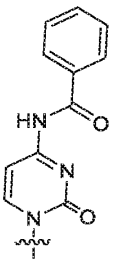
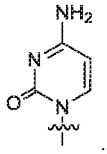
substituted phenyl. In some embodiments, R is phenyl.

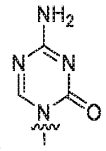
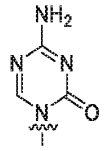
[00366] In some embodiments, R is optionally substituted C_{6-20} arylaliphatic. In some embodiments, R is optionally substituted C_{6-20} arylalkyl. In some embodiments, R is benzyl. In some embodiments, R is optionally substituted C_{6-20} arylheteroaliphatic having 1-10 heteroatoms.

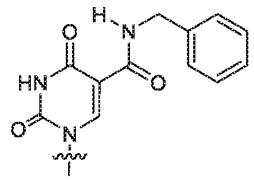
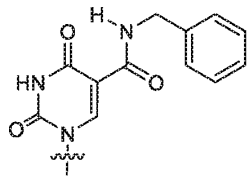
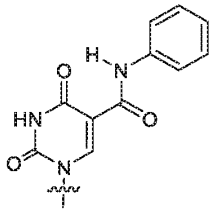
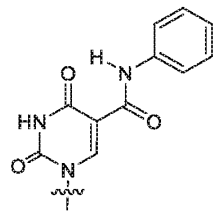
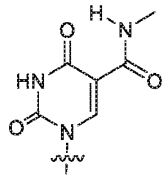
[00367] In some embodiments, R is optionally substituted 5-20 membered heteroaryl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 6-membered heteroaryl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 3-20 membered heterocyclyl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 3-10 membered heterocyclyl having 1-5 heteroatoms. In some embodiments, R is optionally substituted 5-6 membered heterocyclyl having 1-5 heteroatoms. In some embodiments, a heterocyclyl is saturated. In some embodiments, a heterocyclyl is partially saturated.

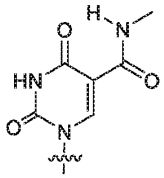
[00368] In some embodiments, a heteroatom is selected from boron, nitrogen, oxygen, sulfur, silicon and phosphorus. In some embodiments, a heteroatom is selected from nitrogen, oxygen, sulfur, and silicon. In some embodiments, a heteroatom is selected from nitrogen, oxygen, and sulfur. In some embodiments, a heteroatom is nitrogen. In some embodiments, a heteroatom is oxygen. In some embodiments, a heteroatom is sulfur.

[00369] As appreciated by those skilled in the art, embodiments described for variables can be readily combined to provide various structures. Those skilled in the art also appreciates that embodiments described for a variable can be readily utilized for other variables that can be that variable, e.g., embodiments of R for R' R^{B2}, R^{B3}, R^{B4}, R^{B5}, R^{B6}, $R^{B2'}$, $R^{B3'}$, $R^{B4'}$, $R^{B5'}$, $R^{B6'}$, etc.; embodiments of embodiments of L^B for L^{B2}, L^{B3}, L^{B4}, L^{B5}, L^{B6}, $L^{B2'}$, $L^{B3'}$, $L^{B4'}$, $L^{B5'}$, $L^{B6'}$, etc. Exemplary embodiments and combinations thereof include but are not limited to structures exemplified herein. Certain examples are described below.

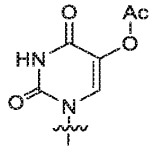
[00370] For example, in some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some

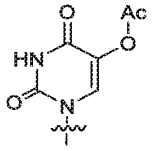
embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

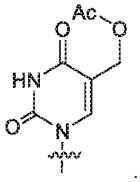
[00371] In some embodiments, X^4 is $-C(O)-$, and O in $-C(O)-$ of X^4 may form a hydrogen bond with a $-H$ of R^5, e.g., a $-H$ in $-NHR'$, $-OH$, or $-SH$ of R^5'. In some embodiments, X^4 is $-C(O)-$, and X^5 is $-C(R^5)=$. In some embodiments, R^5' is $-NHR'$. In some embodiments, R^5 is $-L^{B5}-NHR'$. In some embodiments, L^{B5} is optionally substituted $-CH_2-$. In some embodiments, a methylene unit is replaced with $-C(O)-$. In some embodiments, L^{B5} is $-C(O)-$. In some embodiments, R' is optionally substituted methyl. In some embodiments, R' is $-CH_2Ph$. In some embodiments, R' is optionally substituted phenyl. In some embodiments, R' is phenyl. In some embodiments, R' is optionally substituted C_{1-6} aliphatic. In some embodiments, R' is optionally substituted C_{1-6} alkyl. In some embodiments, R' is optionally substituted methyl. In some embodiments, R' is methyl. In some embodiments, Ring BA is optionally protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally protected . In some

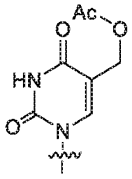


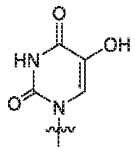
embodiments, Ring BA is . In some embodiments, Ring BA is optionally protected

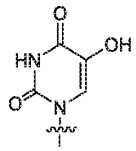


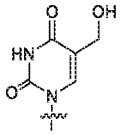
. In some embodiments, Ring BA is . In some embodiments, Ring BA is

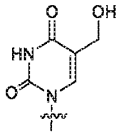


optionally protected . In some embodiments, Ring BA is . In some embodiments,

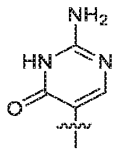


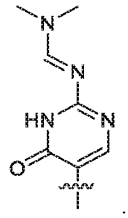
Ring BA is optionally protected . In some embodiments, Ring BA is . In some

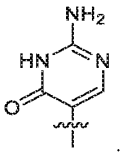
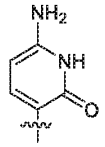
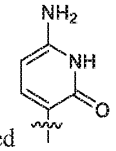
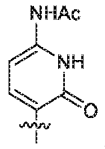
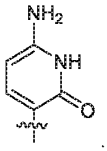


embodiments, Ring BA is optionally protected . In some embodiments, Ring BA is .

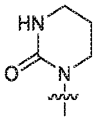
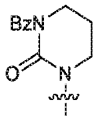
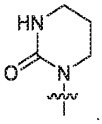
[00372] In some embodiments, X^1 is $-C(-)=$, and X^4 is $=C(-N(R^{B4})_2)-$. In some embodiments, two R groups on the same atom, e.g., a nitrogen atom, are taken together to form optionally substituted $=CH_2$ or $=NH$. In some embodiments, two R groups on the same atom, e.g., a nitrogen atom, are taken together to form optionally substituted $=C(-L^{B4}-R)_2$, $=N-L^{B4}-R$. In some embodiments, a formed group is $=CHN(R)_2$. In some embodiments, a formed group is $=CHN(CH_3)_2$. In some embodiments, X^4 is $=C(-N=CHN(CH_3)_2)-$. In some embodiments, $-N(R^{B4})_2$ is $-NR^{B4}$. In some embodiments, R^{B4} is $-NHC(O)R$. In some embodiments,

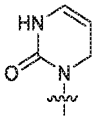
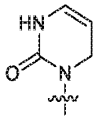


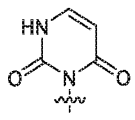
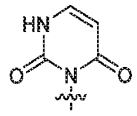
Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

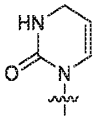
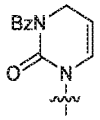
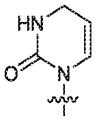
In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is optionally protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is .

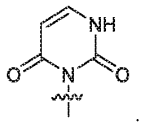
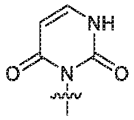
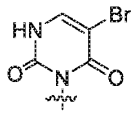
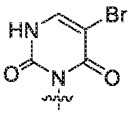
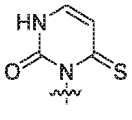
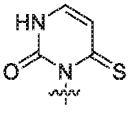
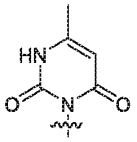
[00373] In some embodiments, X^1 is $-N(-)-$, X^2 is $-C(O)-$, and X^3 is $-N(R^{B3})-$. In some embodiments, X^1 is $-N(-)-$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, and X^4 is $-C(R^{B4})=$. In some embodiments, X^1 is $-N(-)-$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, X^4 is $-C(R^{B4})=$, and X^5 is $-C(R^{B5})=$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

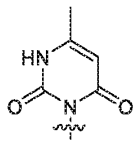
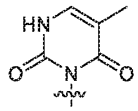
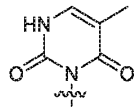
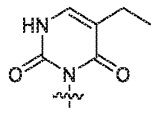
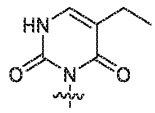
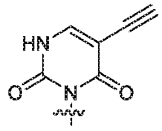
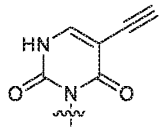
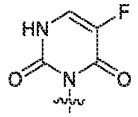
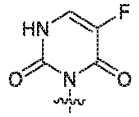
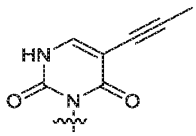
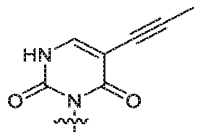
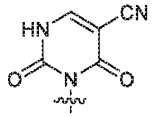
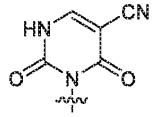
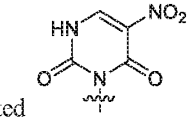
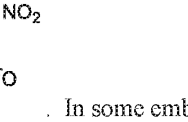
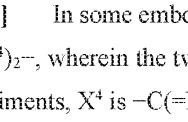
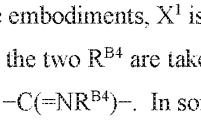
[00374] In some embodiments, X^3 is $-N(R')-$. In some embodiments, R' is $-C(O)R$. In some embodiments, X^4 is $-C(R^{B4})_2-$. In some embodiments, R^{B4} is $-R$. In some embodiments, R^{B4} is $-H$. In some embodiments, X^4 is $-CH_2-$. In some embodiments, X^5 is $-C(R^{B5})_2-$. In some embodiments, R^{B5} is $-R$. In some embodiments, R^{B5} is $-H$. In some embodiments, X^5 is $-CH_2-$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is .

[00375] In some embodiments, X^4 is $-C(R^{B4})=$. In some embodiments, X^4 is $-CH=$. In some embodiments, X^5 is $-C(R^{B5})=$. In some embodiments, X^5 is $-CH=$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some

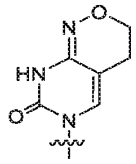
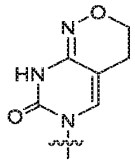
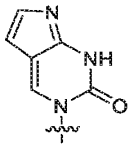
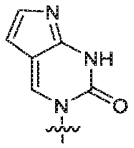
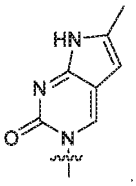
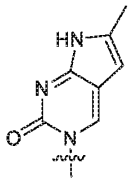
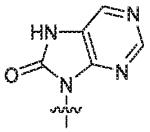
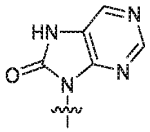
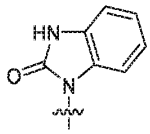
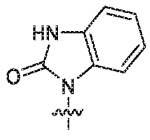
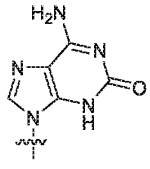
embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

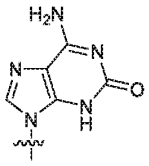
[00376] In some embodiments, X^4 is $-C(R^{B4})_2-$. In some embodiments, X^4 is $-CH_2-$. In some embodiments, X^5 is $-C(R^{B5})=$. In some embodiments, X^5 is $-CH=$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is .

[00377] In some embodiments, X^1 is $-N(-)-$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, X^4 is $-C(R^{B4})=$, X^5 is $-C(R^{B5})=$, X^6 is $-C(O)-$. In some embodiments, X^1 is $-N(-)-$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, X^4 is $-C(R^{B4})=$, X^5 is $-C(R^{B5})=$, X^6 is $-C(S)-$. In some embodiments, each of R^{B3}, R^{B4} and R^{B5} is independently R. In some embodiments, R^{B3} is $-H$. In some embodiments, R^{B4} is $-H$. In some embodiments, R^{B5} is $-H$. In some embodiments, BA is or comprises optionally substituted or protected . In some embodiments, BA is . In some embodiments, BA is or comprises optionally substituted or protected . In some embodiments, BA is . In some embodiments, BA is or comprises optionally substituted or protected . In some embodiments, BA is . In some embodiments, BA is or comprises optionally substituted or protected . In some embodiments,

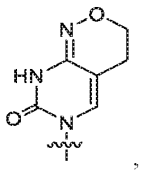
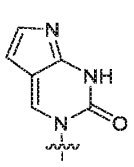
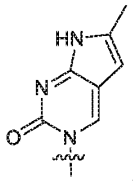
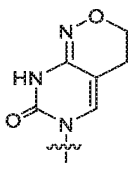
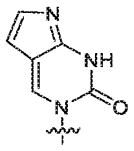
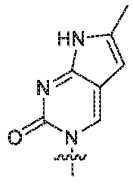
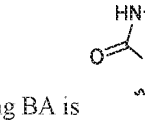
BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  . In some embodiments, BA is or comprises optionally substituted or protected  . In some embodiments, BA is  .

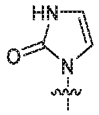
[00378] In some embodiments, X^1 is –N(–)–, X^2 is –C(O)–, X^3 is –N(R^{B3})–. In some embodiments, X^4 is –C(R^{B4})$_2$–, wherein the two R^{B4} are taken together to form =O, or =C(–L^{B4}– R^{B41})$_2$, =N–L^{B4}– R^{B41}. In some embodiments, X^4 is –C(=NR^{B4})–. In some embodiments, X^5 is –C(R^{B5})=. In some embodiments, R^{B41} or R^{B4}

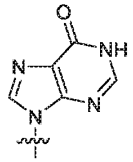
and R^{B5} are R, and are taken together with their intervening atoms to form an optionally substituted ring as described herein. In some embodiment, Ring BA is optionally substituted or protected . In some embodiment, Ring BA is . In some embodiment, Ring BA is optionally substituted or protected . In some embodiment, Ring BA is . In some embodiments, X^1 is –N(–)–, X^2 is –C(O)–, X^3 is –N=. In some embodiments, X^4 is –C(–N(R^{B4})$_2$)=. In some embodiments, X^4 is –C(–NHR^{B4})=. In some embodiments, X^5 is –C(R^{B5})=. In some embodiments, one R^{B4} and R^{B5} are taken together to form an optionally substituted ring as described herein. In some embodiments, a formed ring is an optionally substituted 5-membered ring having a nitrogen atom. In some embodiment, Ring BA is optionally substituted or protected . In some embodiment, Ring BA is . In some embodiment, Ring BA is optionally substituted or protected . In some embodiment, Ring BA is . In some embodiment, Ring BA is optionally substituted or protected . In some embodiment, Ring BA is . In some embodiment, Ring BA is optionally substituted or protected . In

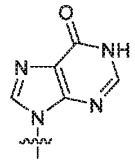
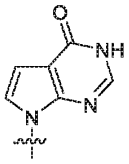
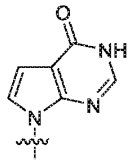
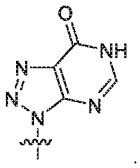
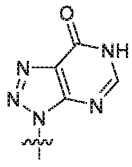
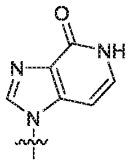
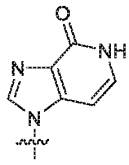
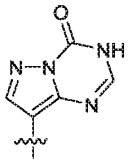
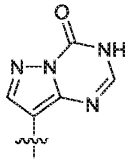
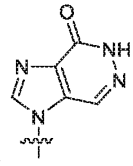
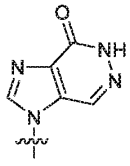
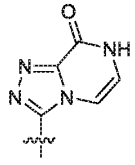
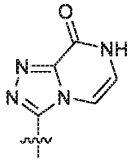


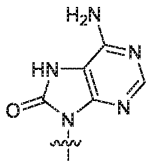
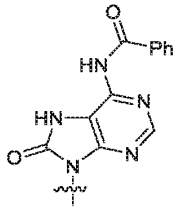
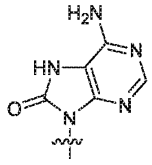
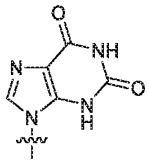
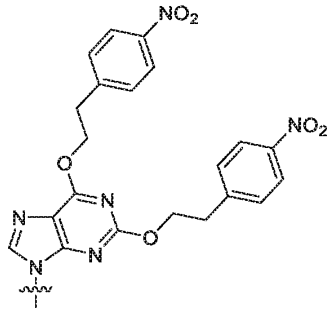
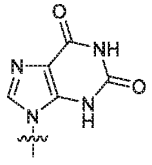
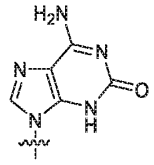
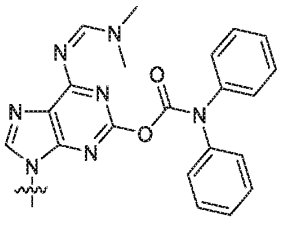
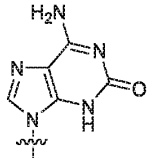
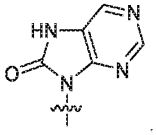
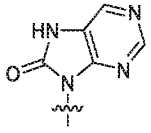
some embodiment, Ring BA is .

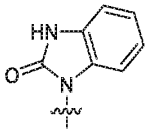
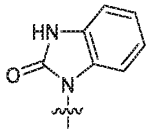
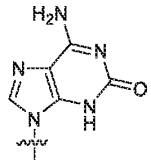
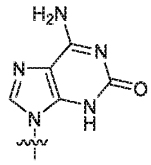
[00379] In some embodiments, Ring BA has the structure of formula BA-IV or BA-V. In some embodiments, X^1 is –N(–)–, X^2 is –C(O)–, and X^3 is –N=. In some embodiments, X^1 is –N(–)–, X^2 is –C(O)–, X^3 is –N=, and X^6 is –C(R^{B6})=. In some embodiments, Ring BA^A is 5-6 membered. In some embodiments, Ring BA^A is monocyclic. In some embodiments, Ring BA^A is partially unsaturated. In some embodiments, Ring BA^A is aromatic. In some embodiments, Ring BA^A has 0-2 heteroatoms. In some embodiments, Ring BA^A has 1-2 heteroatoms. In some embodiments, Ring BA^A has one heteroatom. In some embodiments, Ring BA^A has 2 heteroatoms. In some embodiments, a heteroatom is nitrogen. In some embodiments, heteroatom is oxygen. In some embodiments, Ring BA is optionally substituted or protected , , , or . In some embodiments, Ring BA is , , or .

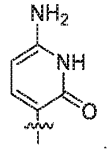
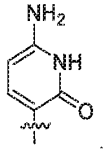
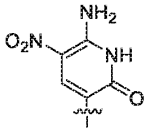
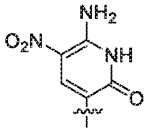
[00380] In some embodiments, Ring BA is an optionally substituted 5-membered ring. In some embodiments, X^1 is bonded to X^5. In some embodiments, each of X^4 and X^5 is independently –CH=. In some embodiments, X^1 is –N(–)–, X^2 is –C(O)–, X^3 is –NH–, X^4 is –CH=, and X^5 is –CH=. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

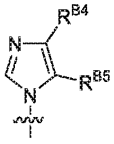
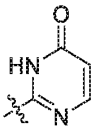
[00381] In some embodiments, Ring BA has the structure of formula BA-VI. In some embodiments, $X^{1'}$ is –N(–)–, $X^{2'}$ is –C(O)– and $X^{3'}$ is –N(R^{B3})–. In some embodiments, $X^{1'}$ is –N(–)–, $X^{2'}$ is –C(O)–, $X^{3'}$ is –N(R^{B3})–, $X^{4'}$ is –C($R^{B4'}$)=, $X^{5'}$ is –N=, $X^{6'}$ is –C($R^{B6'}$)=, and $X^{7'}$ is –N=. In some embodiments, $X^{1'}$ is –N(–)–, $X^{2'}$ is –C(O)–, $X^{3'}$ is –N(R^{B3})–, $X^{4'}$ is –C($R^{B4'}$)=, $X^{5'}$ is –C($R^{B5'}$)=, $X^{6'}$ is –C($R^{B6'}$)=, and $X^{7'}$ is –C($R^{B7'}$)=. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring

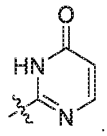
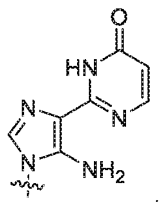
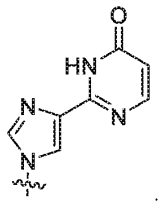
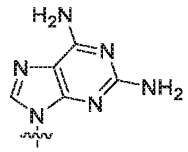
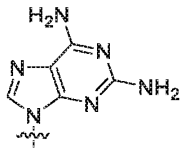
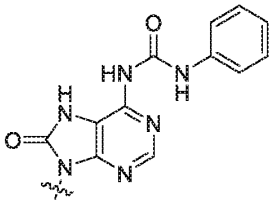
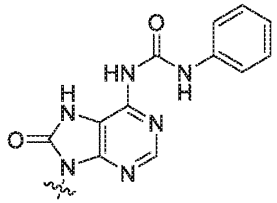
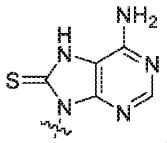
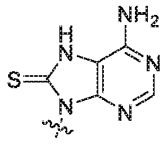
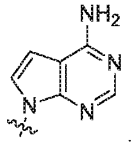
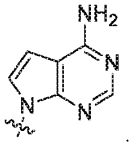
BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected  . In some embodiments, Ring BA is  . In some embodiments, Ring BA is optionally substituted or protected

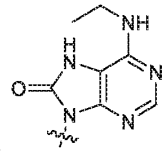
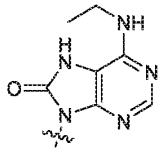
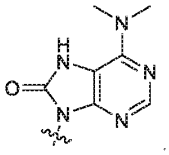
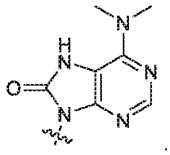
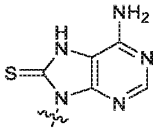
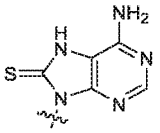
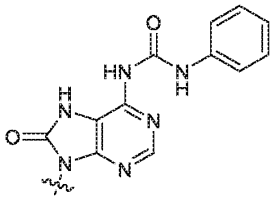
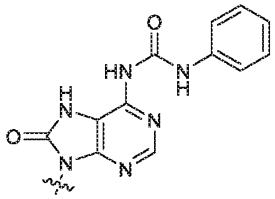
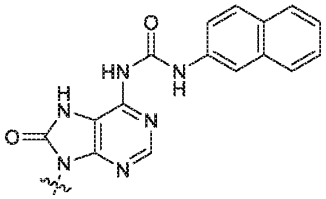
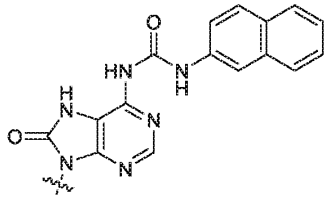
substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA

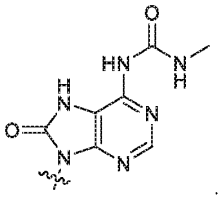
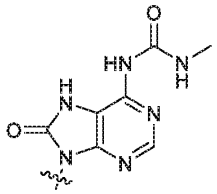
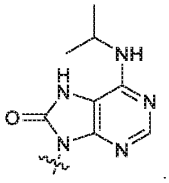
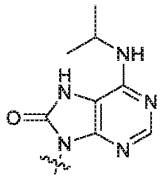
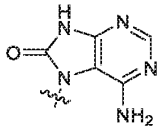
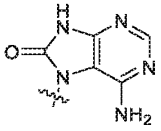
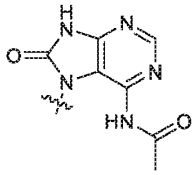
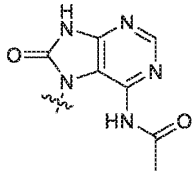
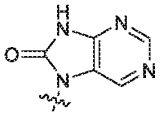
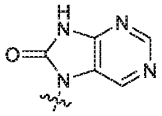
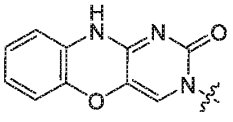
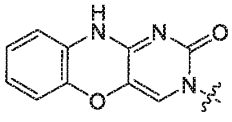
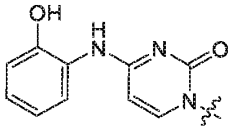
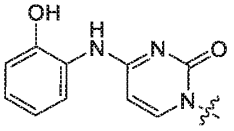
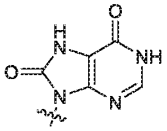
is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, $X^{1'}$ is $-N(-)-$, $X^{2'}$ is $-C(R^{B2'})=$, and $X^{3'}$ is $-N=$. In some embodiments, $X^{1'}$ is $-N(-)-$, $X^{2'}$ is $-C(R^{B2'})=$, $X^{3'}$ is $-N=$, $X^{4'}$ is $-C(-N(R^{B4'})_2)=$, $X^{5'}$ is $-N=$, $X^{6'}$ is $-C(O)-$, and $X^{7'}$ is $-N(R^{B7'})-$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

[00382] In some embodiments, X^1 is $-C(-)=$, X^2 is $-C(O)-$, and X^3 is $-N(R^{B3})-$. In some embodiments, X^1 is $-C(-)=$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, $-C(-N(R^{B4})_2)=$, and X^4 is $-C(R^{B4})=$. In some embodiments, X^1 is $-C(-)=$, X^2 is $-C(O)-$, X^3 is $-N(R^{B3})-$, $-C(-N(R^{B4})_2)=$, X^4 is $-C(R^{B4})=$, and X^6 is $-C(R^{B6})=$. In some embodiments, each of R^{B3}, R^{B4}, and R^{B6} is independently $-H$. In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted or protected . In some embodiments, Ring BA is .

[00383] In some embodiments, Ring BA has the structure of . In some embodiments, R^{B4} is optionally substituted aryl. In some embodiments, R^{B4} is optionally substituted . In some

embodiments, R^{B4} is . In some embodiments, R^{B5} is –H. In some embodiments, R^{B5} is $-N(R')_2$. In some embodiments, R^{B5} is $-NH_2$. In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally

substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted


. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
. In some embodiments, Ring BA is 
. In some embodiments, Ring BA is optionally substituted 
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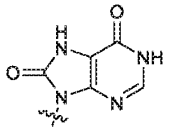
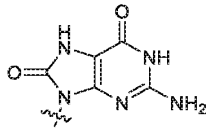
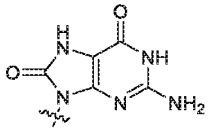
some embodiments, Ring BA is . In some embodiments, Ring BA is optionally substituted . In some embodiments, Ring BA is .

[00384] As described herein, Ring BA may be optionally substituted. In some embodiments, each of X^2, X^3, X^4, X^5, X^6, $X^{2'}$, $X^{3'}$, $X^{4'}$, $X^{5'}$, $X^{6'}$, and $X^{7'}$ is independently and optionally substituted when it is –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, each of X^2, X^3, X^4, X^5, X^6, $X^{2'}$, $X^{3'}$, $X^{4'}$, $X^{5'}$, $X^{6'}$, and $X^{7'}$ is independently and optionally substituted when it is –CH=, –CH_2–, or –NH–. In some embodiments, each of X^2, X^3, X^4, X^5, X^6, $X^{2'}$, $X^{3'}$, $X^{4'}$, $X^{5'}$, $X^{6'}$, and $X^{7'}$ is independently and optionally substituted when it is –CH=. In some embodiments, each of X^2, X^3, X^4, X^5, X^6, $X^{2'}$, $X^{3'}$, $X^{4'}$, $X^{5'}$, $X^{6'}$, and $X^{7'}$ is independently and optionally substituted when it is –CH_2–. In some embodiments, each of X^2, X^3, X^4, X^5, X^6, $X^{2'}$, $X^{3'}$, $X^{4'}$, $X^{5'}$, $X^{6'}$, and $X^{7'}$ is independently and optionally substituted when it is –NH–. In some embodiments, X^2 is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, X^3 is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, X^4 is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, X^5 is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, X^6 is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{2'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{3'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{4'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{5'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{6'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–. In some embodiments, $X^{7'}$ is optionally substituted –CH=, –C(OH)=, –C(–NH_2)=, –CH_2–, –C(=NH)–, or –NH–.

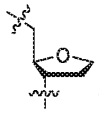
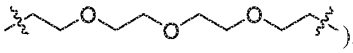
[00385] In some embodiments, $X^{8'}$ is C. In some embodiments, $X^{8'}$ is N. In some embodiments, $X^{9'}$ is C. In some embodiments, $X^{9'}$ is N. In some embodiments, $X^{8'}$ is C and $X^{9'}$ is C. In some embodiments, $X^{8'}$ is C and $X^{9'}$ is N. In some embodiments, $X^{8'}$ is N and $X^{9'}$ is C. In some embodiments, $X^{8'}$ is N and $X^{9'}$ is N.

[00386] In some embodiments, Ring BA is aromatic. In some embodiments, Ring BA is aromatic and has one or more, e.g., 1-5, nitrogen ring atoms. In some embodiments, Ring BA comprises an optionally substituted aromatic ring that has one or more, e.g., 1-5, nitrogen ring atoms.

[00387] As demonstrated herein, in some embodiments provided oligonucleotides comprising certain nucleobases (e.g., b001A, b002A, b008U, C, A, etc.) opposite to target adenosines can among other things

provide improved editing efficiency (e.g., compared to a reference nucleobase such as U). In some embodiments, an opposite nucleoside is linked to an I to its 3' side.

[00388] In some embodiments, a nucleobase is Ring BA as described herein. In some embodiments, an oligonucleotide comprises one or more Ring BA as described herein.

[00389] In some embodiments, an opposite nucleoside is abasic, e.g., having the structure of L010 (), L012 (), or L028 (). As appreciated by those skilled in the art and demonstrated in various oligonucleotides, abasic nucleosides may also be utilized in other portions of oligonucleotides, and oligonucleotides may comprise one or more (e.g., 1, 2, 3, 4, 5, or more), optionally consecutive, abasic nucleosides. In some embodiments, a first domain comprises one or more optionally consecutive, abasic nucleosides. In some embodiments, an oligonucleotide comprises one and no more than one abasic nucleoside. In some embodiments, each abasic nucleoside is independently in a first domain or a first subdomain of a second domain. In some embodiments, each abasic nucleoside is independently in a first domain. In some embodiments, each abasic nucleoside is independently in a first subdomain of a second domain. In some embodiments, an abasic nucleoside is opposite to a target adenosine. As demonstrated herein, a single abasic nucleoside may replace one or more nucleosides each of which independently comprises a nucleobase in a reference oligonucleotide, for example, L010 may be utilized to replace 1 nucleoside which comprises a nucleobase, L012 may be utilized to replace 1, 2 or 3 nucleosides each of which independently comprises a nucleobase, and L028 may be utilized to replace 1, 2 or 3 nucleosides each of which independently comprises a nucleobase. In some embodiments, a basic nucleoside is linked to its 3' immediate nucleoside (which is optionally abasic) through a stereorandom linkage (e.g., a stereorandom phosphorothioate internucleotidic linkage). In some embodiments, each basic nucleoside is independently linked to its 3' immediate nucleoside (which is optionally abasic) through a stereorandom linkage (e.g., a stereorandom phosphorothioate internucleotidic linkage).

[00390] In some embodiments, a modified nucleobase opposite to a target adenine can greatly improve properties and/or activities of an oligonucleotide. In some embodiments, a modified nucleobase at the opposite position can provide high activities even when there is a G next to it (e.g., at the 3' side), and/or other nucleobases, e.g. C, provide much lower activities or virtually no detect activates.

[00391] In some embodiments, a second domain comprises one or more sugars comprising two 2'-H (e.g., natural DNA sugars). In some embodiments, a second domain comprises one or more sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a second domain comprises one or more modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar).

[00392] In some embodiments, a second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars. In some embodiments, a second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently bicyclic sugars (e.g., a LNA sugar) or a 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5. In some embodiments, the number is 6. In some embodiments, the number is 7. In some embodiments, the number is 8. In some embodiments, the number is 9. In some embodiments, the number is 10. In some embodiments, the number is 11. In some embodiments, the number is 12. In some embodiments, the number is 13. In some embodiments, the number is 14. In some embodiments, the number is 15. In some embodiments, the number is 16. In some embodiments, the number is 17. In some embodiments, the number is 18. In some embodiments, the number is 19. In some embodiments, the number is 20. In some embodiments, R is methyl.

[00393] In some embodiments, about 5%-100%, (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a second domain are independently a modified sugar. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a second domain are independently a bicyclic sugar (e.g., a LNA sugar) or a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%,

65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a second domain are independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, R is methyl.

[00394] In some embodiments, a second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently with a modification that is not 2'-F. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a second domain are independently modified sugars with a modification that is not 2'-F. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a second domain are independently modified sugars with a modification that is not 2'-F. In some embodiments, modified sugars of a second domain are each independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00395] In some embodiments, a second domain comprises one or more 2'-F modified sugars. In some embodiments, a second domain comprises no 2'-F modified sugars. In some embodiments, a second domain comprises one or more bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H. In some embodiments, levels of bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H, individually or combined, are relatively high compared to level of 2'-F modified sugars. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%,

60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a second domain comprises 2'-F. In some embodiments, no more than about 50% of sugars in a second domain comprises 2'-F. In some embodiments, a second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-$N(R)_2$ modification. In some embodiments, a second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-NH_2 modification. In some embodiments, a second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) bicyclic sugars, e.g., LNA sugars. In some embodiments, a second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

[00396] In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a second domain comprises 2'-MOE. In some embodiments, no more than about 50% of sugars in a second domain comprises 2'-MOE. In some embodiments, no sugars in a second domain comprises 2'-MOE.

[00397] In some embodiments, a second domain comprise about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a second domain are modified internucleotidic linkages. In some embodiments, each internucleotidic linkage in a second domain is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PS internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PN internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a neutral internucleotidic linkage, e.g., n001. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or

about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a second domain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a second domain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a second domain is chirally controlled. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a second domain is *Sp*. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) phosphorothioate internucleotidic linkages in a second domain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a second domain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a second domain is *Sp*. In some embodiments, the number is one or more. In some embodiments, the number is 2 or more. In some embodiments, the number is 3 or more. In some embodiments,

the number is 4 or more. In some embodiments, the number is 5 or more. In some embodiments, the number is 6 or more. In some embodiments, the number is 7 or more. In some embodiments, the number is 8 or more. In some embodiments, the number is 9 or more. In some embodiments, the number is 10 or more. In some embodiments, the number is 11 or more. In some embodiments, the number is 12 or more. In some embodiments, the number is 13 or more. In some embodiments, the number is 14 or more. In some embodiments, the number is 15 or more. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, each internucleotidic linkage linking two second domain nucleosides is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage of a second domain is bonded to two nucleosides of the second domain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a first domain and a nucleoside in a second domain may be properly considered an internucleotidic linkage of a second domain. In some embodiments, it was observed that a high percentage (e.g., relative to *Rp* internucleotidic linkages and/or natural phosphate linkages) of *Sp* internucleotidic linkages provide improved properties and/or activities, e.g., high stability and/or high adenosine editing activity.

[00398] In some embodiments, a second domain comprises a certain level of *Rp* internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in a second domain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-

85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in a second domain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in a second domain. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 1-5, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *R*p chiral internucleotidic linkages. In some embodiments, the number is about or no more than about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the number is about or no more than about 3. In some embodiments, the number is about or no more than about 4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10.

[00399] In some embodiments, each phosphorothioate internucleotidic linkage in a second domain is independently chirally controlled. In some embodiments, each is independently *S*p or *R*p. In some embodiments, a high level is *S*p as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a second domain is chirally controlled and is *S*p. In some embodiments, one or more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5) is *R*p.

[00400] In some embodiments, each phosphorothioate internucleotidic linkage in a second domain is

independently chirally controlled. In some embodiments, each is independently *Sp* or *Rp*. In some embodiments, a high level is *Sp* as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a second domain is chirally controlled and is *Sp*. In some embodiments, one or more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5) is *Rp*.

[00401] In some embodiments, as illustrated in certain examples, a second domain comprises one or more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Rp*. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Sp*. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in a second domain is about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, it is about 1. In some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in a second domain are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more (e.g., about 2, about 3, about 4 etc.) consecutive non-negatively charged internucleotidic linkages, are at the 3'-end of a second domain. In some embodiments, the last two or three or four internucleotidic linkages of a second domain comprise at least one internucleotidic linkage that is not a non-negatively charged internucleotidic linkage. In some embodiments, the last two or three or four internucleotidic linkages of a second domain comprise at least one internucleotidic linkage that is not n001.

[00402] In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second domain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second domain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second domain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second domain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second domain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the last two nucleosides of a second domain are the last two nucleosides of an oligonucleotide. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second domain is a non-negatively charged internucleotidic linkage. In some

embodiments, the internucleotidic linkage linking the first two nucleosides of a second domain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second domain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second domain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second domain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage such as n001.

[00403] In some embodiments, a first domain comprises one or more PO internucleotidic linkages. In some embodiments, a second domain comprises one or more natural phosphate linkages. In some embodiments, a second domain contains no PO internucleotidic linkages. In some embodiments, a second domain contains no natural phosphate linkages.

[00404] In some embodiments, a second domain recruits, promotes or contribute to recruitment of, a protein such as an ADAR protein. In some embodiments, a second domain recruits, or promotes or contribute to interactions with, a protein such as an ADAR protein. In some embodiments, a second domain contacts with a RNA binding domain (RBD) of ADAR. In some embodiments, a second domain contacts with a catalytic domain of ADAR which has a deaminase activity. In some embodiments, various nucleobases, sugars and/or internucleotidic linkages may interact with one or more residues of proteins, e.g., ADAR proteins.

[00405] In some embodiments, a second domain comprises or consists of a first subdomain as described herein. In some embodiments, a second domain comprises or consists of a second subdomain as described herein. In some embodiments, a second domain comprises or consists of a third subdomain as described herein. In some embodiments, a second domain comprises or consists of a first subdomain, a second subdomain and a third subdomain from 5' to 3'. Certain embodiments of such subdomains are described below.

First Subdomains

[00406] As described herein, in some embodiment, an oligonucleotide comprises a first domain and a second domain from 5' to 3'. In some embodiments, a second domain comprises or consists of a first subdomain, a second subdomain, and a third subdomain from 5' to 3'. Certain embodiments of a first subdomain are described below as examples. In some embodiments, a first subdomain comprise a nucleoside opposite to target adenosine to be modified (e.g., conversion to I).

[00407] In some embodiments, a first subdomain has a length of about 1-50, 1-40, 1-30, 1-20 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a first subdomain has a length of about 5-30 nucleobases. In some embodiments, a first subdomain has a length of about 10-30 nucleobases. In some embodiments, a first subdomain has a length of about 10-20 nucleobases. In some embodiments, a first subdomain has a length of about 5-15 nucleobases. In some embodiments, a first subdomain has a length of about 13-16 nucleobases. In some embodiments, a first subdomain has a length of about 6-12 nucleobases. In some embodiments, a first

subdomain has a length of about 6-9 nucleobases. In some embodiments, a first subdomain has a length of about 1-10 nucleobases. In some embodiments, a first subdomain has a length of about 1-7 nucleobases. In some embodiments, a first subdomain has a length of about 1-5 nucleobases. In some embodiments, a first subdomain has a length of about 1-3 nucleobases. In some embodiments, a first subdomain has a length of 1 nucleobase. In some embodiments, a first subdomain has a length of 2 nucleobases. In some embodiments, a first subdomain has a length of 3 nucleobases. In some embodiments, a first subdomain has a length of 4 nucleobases. In some embodiments, a first subdomain has a length of 5 nucleobases. In some embodiments, a first subdomain has a length of 6 nucleobases. In some embodiments, a first subdomain has a length of 7 nucleobases. In some embodiments, a first subdomain has a length of 8 nucleobases. In some embodiments, a first subdomain has a length of 9 nucleobases. In some embodiments, a first subdomain has a length of 10 nucleobases. In some embodiments, a first subdomain has a length of 11 nucleobases. In some embodiments, a first subdomain has a length of 12 nucleobases. In some embodiments, a first subdomain has a length of 13 nucleobases. In some embodiments, a first subdomain has a length of 14 nucleobases. In some embodiments, a first subdomain has a length of 15 nucleobases.

[00408] In some embodiments, a first subdomain is about, or at least about, 5-95%, 10%-90%, 20%-80%, 30%-70%, 40%-70%, 40%-60%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% of a second domain. In some embodiments, a percentage is about 30%-80%. In some embodiments, a percentage is about 30%-70%. In some embodiments, a percentage is about 40%-60%. In some embodiments, a percentage is about 20%. In some embodiments, a percentage is about 25%. In some embodiments, a percentage is about 30%. In some embodiments, a percentage is about 35%. In some embodiments, a percentage is about 40%. In some embodiments, a percentage is about 45%. In some embodiments, a percentage is about 50%. In some embodiments, a percentage is about 55%. In some embodiments, a percentage is about 60%. In some embodiments, a percentage is about 65%. In some embodiments, a percentage is about 70%. In some embodiments, a percentage is about 75%. In some embodiments, a percentage is about 80%. In some embodiments, a percentage is about 85%. In some embodiments, a percentage is about 90%.

[00409] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches exist in a first subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches. In some embodiments, there are 10 mismatches.

[00410] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles exist in a first subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 wobble. In some embodiments, there are 2 wobbles. In some embodiments, there are

3 wobbles. In some embodiments, there are 4 wobbles. In some embodiments, there are 5 wobbles. In some embodiments, there are 6 wobbles. In some embodiments, there are 7 wobbles. In some embodiments, there are 8 wobbles. In some embodiments, there are 9 wobbles. In some embodiments, there are 10 wobbles.

[00411] In some embodiments, duplexes of oligonucleotides and target nucleic acids in a first subdomain region comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00412] In some embodiments, a first subdomain is fully complementary to a target nucleic acid.

[00413] In some embodiments, a first subdomain comprises one or more modified nucleobases.

[00414] In some embodiments, a first subdomain comprise a nucleoside opposite to a target adenosine, e.g., when the oligonucleotide forms a duplex with a target nucleic acid. Suitable nucleobases including modified nucleobases in opposite nucleosides are described herein. For example, in some embodiment, an opposite nucleobase is optionally substituted or protected nucleobase selected from C, a tautomer of C, U, a tautomer of U, A, a tautomer of A, and a nucleobase which is or comprises Ring BA having the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA.

[00415] In some embodiments, a first subdomain comprises one or more sugars comprising two 2'-H (e.g., natural DNA sugars). In some embodiments, a first subdomain comprises one or more sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a first subdomain comprises one or more modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar).

[00416] In some embodiments, a first subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars. In some embodiments, a first subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently bicyclic sugars (e.g., a LNA sugar) or a 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a first subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10

(e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5. In some embodiments, the number is 6. In some embodiments, the number is 7. In some embodiments, the number is 8. In some embodiments, the number is 9. In some embodiments, the number is 10. In some embodiments, the number is 11. In some embodiments, the number is 12. In some embodiments, the number is 13. In some embodiments, the number is 14. In some embodiments, the number is 15. In some embodiments, the number is 16. In some embodiments, the number is 17. In some embodiments, the number is 18. In some embodiments, the number is 19. In some embodiments, the number is 20. In some embodiments, R is methyl.

[00417] In some embodiments, about 5%-100%, (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a first subdomain are independently a modified sugar. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a first subdomain are independently a bicyclic sugar (e.g., a LNA sugar) or a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a first subdomain are independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a

percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, R is methyl.

[00418] In some embodiments, a first subdomain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently with a modification that is not 2'-F. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first subdomain are independently modified sugars with a modification that is not 2'-F. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first subdomain are independently modified sugars with a modification that is not 2'-F. In some embodiments, modified sugars of a first subdomain are each independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a first domain is a 2'-F modified sugar.

[00419] In some embodiments, a first subdomain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first subdomain are independently modified sugars selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some

embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a first subdomain are independently modified sugars selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00420] In some embodiments, each sugar in a first subdomain independently comprises a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a first subdomain independently comprises a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $-CH_2-$. In some embodiments, each sugar in a first subdomain independently comprises 2'-OMe.

[00421] In some embodiments, a first subdomain comprises one or more 2'-F modified sugars. In some embodiments, a first subdomain comprises no 2'-F modified sugars. In some embodiments, a first subdomain comprises one or more bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) 2'-OMe modified sugars. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) consecutive 2'-OMe modified sugars. In some embodiments, levels of bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H, individually or combined, are relatively high compared to level of 2'-F modified sugars. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first subdomain comprises 2'-F. In some embodiments, no more than about 50% of sugars in a first subdomain comprises 2'-F. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-$N(R)_2$ modification. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-NH_2 modification. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) bicyclic sugars, e.g., LNA sugars. In some embodiments, a first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

[00422] In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a first subdomain comprises 2'-MOE. In some embodiments, no more than about 50% of sugars in a first subdomain comprises 2'-MOE. In some embodiments, no sugars in a first subdomain comprises 2'-MOE.

[00423] In some embodiments, a first subdomain contains more 2'-OR modified sugars than 2'-F modified sugars. In some embodiments, each sugar in a first subdomain is independently a 2'-OR modified sugar or a 2'-F modified sugar. In some embodiments, a first subdomain contains only 3 nucleosides, two of which are independently 2'-OR modified sugars and one is a 2'-F modified sugar. In some embodiments, the 2'-F modified nucleoside is at the 3'-end of the first subdomain and connects to a second subdomain. In some embodiments, each 2'-OR modified sugar is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, or a 2'--O--L^B--4' modification. In some embodiments, each 2'-OR modified sugar is independently 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE modified sugar. In some embodiments, a sugar is 2'-OMe modified and a sugar is 2'-MOE. In some embodiments, a first subdomain contains only 3 nucleosides which are N_2, N_3 and N_4.

[00424] In some embodiments, a first subdomain comprise about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a first subdomain are modified internucleotidic linkages. In some embodiments, each internucleotidic linkage in a first subdomain is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PS internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PN internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a neutral internucleotidic linkage, e.g., n001. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10,

11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a first subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a first subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a first subdomain is chirally controlled. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a first subdomain is *Sp*. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) phosphorothioate internucleotidic linkages in a first subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a first subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a first subdomain is *Sp*. In some embodiments, the number is one or more. In some embodiments, the number is 2

or more. In some embodiments, the number is 3 or more. In some embodiments, the number is 4 or more. In some embodiments, the number is 5 or more. In some embodiments, the number is 6 or more. In some embodiments, the number is 7 or more. In some embodiments, the number is 8 or more. In some embodiments, the number is 9 or more. In some embodiments, the number is 10 or more. In some embodiments, the number is 11 or more. In some embodiments, the number is 12 or more. In some embodiments, the number is 13 or more. In some embodiments, the number is 14 or more. In some embodiments, the number is 15 or more. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, each internucleotidic linkage linking two first subdomain nucleosides is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage of a first subdomain is bonded to two nucleosides of the first subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a first subdomain and a nucleoside in a second subdomain may be properly considered an internucleotidic linkage of a first subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a first subdomain and a nucleoside in a second subdomain is a modified internucleotidic linkage; in some embodiments, it is a chiral internucleotidic linkage; in some embodiments, it is chirally controlled; in some embodiments, it is *Rp*; in some embodiments, it is *Sp*.

[00425] In some embodiments, a first subdomain comprises a certain level of *Rp* internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in a first subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-

80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in a first subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in a first subdomain. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 1-5, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *R*p chiral internucleotidic linkages. In some embodiments, the number is about or no more than about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the number is about or no more than about 3. In some embodiments, the number is about or no more than about 4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10.

[00426] In some embodiments, each phosphorothioate internucleotidic linkage in a first subdomain is independently chirally controlled. In some embodiments, each is independently *S*p or *R*p. In some embodiments, a high level is *S*p as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a first subdomain is chirally controlled and is *S*p. In some embodiments, one or

more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5) is *R*p.

[00427] In some embodiments, as illustrated in certain examples, a first subdomain comprises one or more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *R*p. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *S*p. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in a first subdomain is about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, it is about 1. In some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in a first subdomain are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more (e.g., about 2, about 3, about 4 etc.) consecutive non-negatively charged internucleotidic linkages, are at the 3'-end of a first subdomain. In some embodiments, the last two or three or four internucleotidic linkages of a first subdomain comprise at least one internucleotidic linkage that is not a non-negatively charged internucleotidic linkage. In some embodiments, the last two or three or four internucleotidic linkages of a first subdomain comprise at least one internucleotidic linkage that is not n001. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first subdomain is a *S*p non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first subdomain is a *R*p non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a first subdomain is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first subdomain is a *S*p non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first subdomain is a *R*p non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a first subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic

linkage linking the first two nucleosides of a first subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage such as n001.

[00428] In some embodiments, a first subdomain comprises one or more PO internucleotidic linkages. In some embodiments, a first subdomain comprises one or more natural phosphate linkages. In some embodiments, a first subdomain contains no natural phosphate linkages. In some embodiments, one or more 2'-OR modified sugars wherein R is not –H are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-OMe modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, one or more 2'-MOE modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, each 2'-MOE modified sugar is independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-OR modified sugars wherein R is not –H are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-OMe modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) 2'-MOE modified sugars are independently bonded to a natural phosphate linkage. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) internucleotidic linkages bonded to two 2'-OR modified sugars are independently natural phosphate linkages. In some embodiments, 50% or more (e.g., 50%-100%, 50%-90%, 50-80%, or about 50%, 60%, 66%, 70%, 75%, 80%, 90% or more) internucleotidic linkages bonded to two 2'-OMe or 2'-MOE modified sugars are independently natural phosphate linkages.

[00429] In some embodiments, a first subdomain comprises a 5'-end portion, e.g., one having a length of about 1-20, 1-15, 1-10, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleobases. In some embodiments, a 5'-end portion has a length of about 3-6 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases. In some embodiments, a length is 6 nucleobases. In some embodiments, a length is 7 nucleobases. In some embodiments, a length is 8 nucleobases. In some embodiments, a length is 9 nucleobases. In some embodiments, a length is 10 nucleobases. In some embodiments, a 5'-end portion comprises the 5'-end nucleobase of a first subdomain.

[00430] In some embodiments, a 5'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 5'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-20, 1-15, 1-10, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 5'-end portion are independently modified sugars. In some

embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 5'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00431] In some embodiments, one or more of the modified sugars independently comprises 2'-F or 2'-OR, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, one or more of the modified sugars are independently 2'-F or 2'-OMe. In some embodiments, each modified sugar in a 5'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl.

[00432] In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are *R*p. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are *S*p. In some embodiments, each internucleotidic linkage of a 5'-end portion is *S*p.

[00433] In some embodiments, a 5'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) mismatches as described herein. In some embodiments, a 5'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) wobbles as described herein. In some embodiments, a 5'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00434] In some embodiments, a first subdomain comprises a 3'-end portion, e.g., one having a length of about 1-20, 1-15, 1-10, 1-5, 1-3, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleobases. In some embodiments, a 3'-end portion has a length of about 1-3 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases. In some embodiments, a length is 6 nucleobases. In some embodiments, a length is 7 nucleobases. In some embodiments, a length is 8 nucleobases. In some embodiments, a length is 9 nucleobases. In some embodiments, a length is 10 nucleobases. In some embodiments, a 3'-end portion comprises the 3'-end nucleobase of a first subdomain. In some embodiments, a first subdomain comprises or consists of a 5'-end portion and a 3'-end portion.

[00435] In some embodiments, a 5'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 5'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-20, 1-15, 1-10, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00436] In some embodiments, one or more of the modified sugars independently comprises 2'-F or 2'-OR, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, one or more of the modified sugars are independently 2'-F or 2'-OMe. In some embodiments, each modified sugar in a 5'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl.

[00437] In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a higher level (in numbers and/or percentage) of 2'-F modified sugars and/or sugars comprising two 2'-H (e.g., natural DNA sugars), and/or a lower level (in numbers and/or percentage) of other types of modified sugars, e.g., bicyclic

sugars and/or sugars with 2'-OR modifications wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a higher level of 2'-F modified sugars and/or a lower level of 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a higher level of 2'-F modified sugars and/or a lower level of 2'-OMe modified sugars. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a lower level of 2'-F modified sugars and/or a higher level of 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a lower level of 2'-F modified sugars and/or a higher level of 2'-OMe modified sugars. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a higher level of natural DNA sugars and/or a lower level of 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 5'-end portion, a 3'-end portion contains a higher level of natural DNA sugars and/or a lower level of 2'-OMe modified sugars. In some embodiments, a 3'-end portion contains low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of modified sugars which are bicyclic sugars or sugars comprising 2'-OR wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl). In some embodiments, a 3'-end portion contains no modified sugars which are bicyclic sugars or sugars comprising 2'-OR wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl).

[00438] In some embodiments, one or more modified sugars independently comprise 2'-F. In some embodiments, no modified sugars comprises 2'-OMe or other 2'-OR modifications wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar of a 3'-end portion independently comprises two 2'-H or a 2'-F modification. In some embodiments, a 3'-end portion comprises 1, 2, 3, 4, or 5 2'-F modified sugars. In some embodiments, a 3'-end portion comprises 1-3 2'-F modified sugars. In some embodiments, a 3'-end portion comprises 1, 2, 3, 4, or 5 natural DNA sugars. In some embodiments, a 3'-end portion comprises 1-3 natural DNA sugars.

[00439] In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are *Rp*. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are *Sp*. In some embodiments, each internucleotidic linkage of a 3'-end portion is *Sp*. In some embodiments, a 3'-end portion contains a higher level (in number and/or percentage) of *Rp* internucleotidic linkage and/or natural phosphate linkage compared to a 5'-end portion.

[00440] In some embodiments, a 3'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) mismatches as described herein. In some embodiments, a 3'-end portion comprises one

or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) wobbles as described herein. In some embodiments, a 3'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00441] In some embodiments, a first subdomain recruits, promotes or contribute to recruitment of, a protein such as an ADAR protein, e.g., ADAR1, ADAR2, etc. In some embodiments, a first subdomain recruits, or promotes or contribute to interactions with, a protein such as an ADAR protein. In some embodiments, a first subdomain contacts with a RNA binding domain (RBD) of ADAR. In some embodiments, a first subdomain contacts with a catalytic domain of ADAR which has a deaminase activity. In some embodiments, a first subdomain contact with a domain that has a deaminase activity of ADAR1. In some embodiments, a first subdomain contact with a domain that has a deaminase activity of ADAR2. In some embodiments, various nucleobases, sugars and/or internucleotidic linkages of a first subdomain may interact with one or more residues of proteins, e.g., ADAR proteins.

Second Subdomains

[00442] As described herein, in some embodiment, an oligonucleotide comprises a first domain and a second domain from 5' to 3'. In some embodiments, a second domain comprises or consists of a first subdomain, a second subdomain, and a third subdomain from 5' to 3'. Certain embodiments of a second subdomain are described below as examples. In some embodiments, a second subdomain comprise a nucleoside opposite to a target adenosine to be modified (e.g., conversion to I). In some embodiments, a second subdomain comprises one and no more than one nucleoside opposite to a target adenosine. In some embodiments, each nucleoside opposite to a target adenosine of an oligonucleotide is in a second subdomain.

[00443] In some embodiments, a second subdomain has a length of about 1-10, 1-5, 1-3, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleobases. In some embodiments, a second subdomain has a length of about 1-10 nucleobases. In some embodiments, a second subdomain has a length of about 1-5 nucleobases. In some embodiments, a second subdomain has a length of about 1-3 nucleobases. In some embodiments, a second subdomain has a length of 1 nucleobase. In some embodiments, a second subdomain has a length of 2 nucleobases. In some embodiments, a second subdomain has a length of 3 nucleobases. In some embodiments, all the nucleosides in a second subdomain are 5'-$N_1N_0N_{-1}$-3'.

[00444] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches exist in a second subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches.

In some embodiments, there are 10 mismatches.

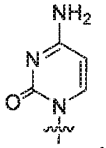
[00445] In some embodiments, a second subdomain comprises one and no more than one mismatch. In some embodiments, a second subdomain comprises two and no more than two mismatches. In some embodiments, a second subdomain comprises two and no more than two mismatches, wherein one mismatch is between a target adenosine and its opposite nucleoside, and/or one mismatch is between a nucleoside next to a target adenosine and its corresponding nucleoside in an oligonucleotide. In some embodiments, a mismatch between a nucleoside next to a target adenosine and its corresponding nucleoside in an oligonucleotide is a wobble. In some embodiments, a wobble is I-C. In some embodiments, C is next to a target adenosine, e.g., immediately to its 3' side.

[00446] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles exist in a second subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 wobble. In some embodiments, there are 2 wobbles. In some embodiments, there are 3 wobbles. In some embodiments, there are 4 wobbles. In some embodiments, there are 5 wobbles. In some embodiments, there are 6 wobbles. In some embodiments, there are 7 wobbles. In some embodiments, there are 8 wobbles. In some embodiments, there are 9 wobbles. In some embodiments, there are 10 wobbles.

[00447] In some embodiments, duplexes of oligonucleotides and target nucleic acids in a second subdomain region comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00448] In some embodiments, a second subdomain is fully complementary to a target nucleic acid.

[00449] In some embodiments, a second subdomain comprises one or more modified nucleobases.

[00450] In some embodiments, a second subdomain comprise a nucleoside opposite to a target adenosine, e.g., when the oligonucleotide forms a duplex with a target nucleic acid. Suitable nucleobases including modified nucleobases in opposite nucleosides are described herein. For example, in some embodiment, an opposite nucleobase is optionally substituted or protected nucleobase selected from C, a tautomer of C, U, a tautomer of U, A, a tautomer of A, and a nucleobase which is or comprises Ring BA having the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA. For example, in some embodiments, an opposite nucleobase is selected from 

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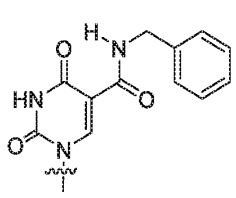
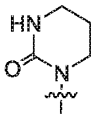
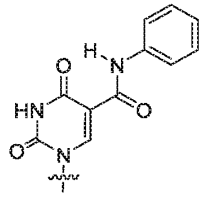
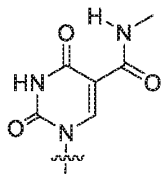
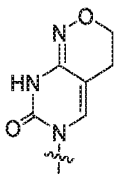
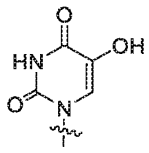
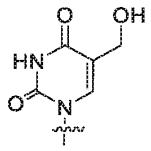
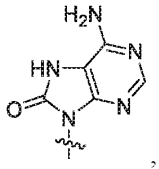
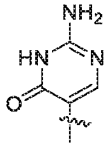
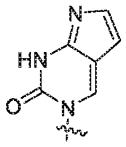
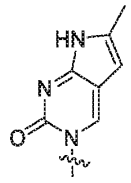
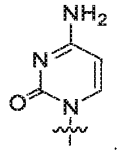
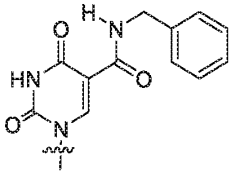
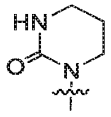
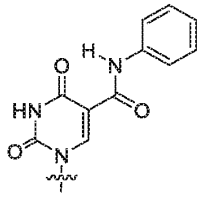
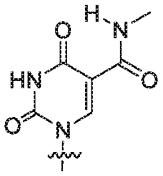
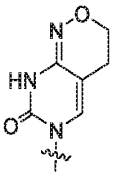
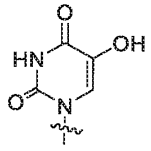
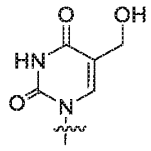
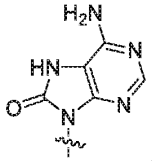
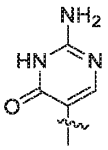
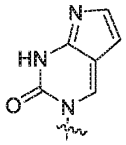
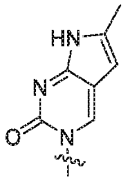
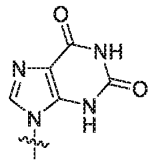
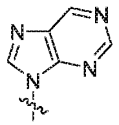
, , , , , , , , , , or . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is . In some

embodiments, an opposite nucleobase is . In some embodiments, an opposite nucleobase is or



[00451] In some embodiments, a second subdomain comprises a modified nucleobase next to an opposite nucleobase. In some embodiments, it is to the 5' side. In some embodiments, it is to the 3' side. In some embodiments, on each side there is independently a modified nucleobase. Among other things, the present disclosure recognizes that nucleobases adjacent to (e.g., next to) opposite nucleobases may cause disruption (e.g., steric hindrance) to recognition, binding, interaction, and/or modification of target nucleic acids, oligonucleotides and/or duplexes thereof. In some embodiments, disruption is associated with an adjacent G. In some embodiments, the present disclosure provides nucleobases that can replace G and provide improved stability and/or activities compared to G. For example, in some embodiments, an adjacent nucleobase (e.g., 3'-immediate nucleoside of an opposite nucleoside) is hypoxanthine (replacing G to reduce disruption (e.g., steric hindrance) and/or forming wobble base pairing with C). In some embodiments, an adjacent nucleobase is a derivative of hypoxanthine. In some embodiments, 3'-immediate nucleoside comprises a nucleobase which is or comprise Ring BA having the structure of formula BA-VI. In some embodiments, an adjacent nucleobase is . In some embodiments, an adjacent nucleobase is . In some embodiments, the present disclosure provides flexibility, e.g., with respect to nucleobases that can be utilized in 3'-immediate nucleosides of opposite nucleosides. In some embodiments, the present disclosure provides various modified nucleobases that can be utilized in opposite nucleosides and can allow utilization of G (e.g., opposite to C) in 3'-immediate nucleosides of opposite nucleosides without significantly reducing editing levels. In some embodiments, a nucleobase at N_0 is BA which has the structure of formula BA-III-e as described herein. In some embodiments, a nucleobase at N_0 is BA which has the structure of formula BA-VI as described herein. For example, in some embodiments, high and at least comparable editing was observed with b008U in N_0 and G in N_{-1} and opposite to C. In some embodiments, high and at least comparable editing was observed with b001A in N_0 and G in N_{-1} and opposite to C.

[00452] In some embodiments, a second subdomain comprises one or more sugars comprising two 2'-H (e.g., natural DNA sugars). In some embodiments, a second subdomain comprises one or more sugars

comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a second subdomain comprises one or more modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar). In some embodiments, an opposite nucleoside comprises an acyclic sugar such as an UNA sugar. In some embodiments, such an acyclic sugar provides flexibility for proteins to perform modifications on a target adenosine.

[00453] In some embodiments, a second subdomain comprises about 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) modified sugars independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a second subdomain are independently modified sugars selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00454] In some embodiments, low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a second subdomain independently comprise a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a second subdomain independently contains no 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $–CH_2–$. In some embodiments, each sugar in a second subdomain independently contains no 2'-OMe.

[00455] In some embodiments, high levels (e.g., more than 50%, 60%, 70%, 80%, 90%, or 95%, 99%, or more than 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20) of sugars in a second subdomain independently comprise a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a second subdomain independently contains a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $–CH_2–$. In some embodiments, each sugar in a second subdomain independently comprises 2'-OMe.

[00456] In some embodiments, a second subdomain comprises one or more 2'-F modified sugars.

[00457] In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a second subdomain are independently 2'-F modified sugars, sugars comprising two 2'-H (e.g., natural DNA sugars), or sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a second subdomain are independently 2'-F modified sugars,

natural DNA sugars, or natural RNA sugars. In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a second subdomain are independently 2'-F modified sugars and natural DNA sugars. In some embodiments, a level is 100%. In some embodiments, a second subdomain comprise 1, 2, 3, 4 or 5 2'-F modified sugars. In some embodiments, a second subdomain comprise 1, 2, 3, 4 or 5 sugars comprising two 2'-H. In some embodiments, a second subdomain comprise 1, 2, 3, 4 or 5 natural DNA sugars. In some embodiments, a second subdomain comprise 1, 2, 3, 4 or 5 sugars comprising 2'-OH. In some embodiments, a second subdomain comprise 1, 2, 3, 4 or 5 natural RNA sugars. In some embodiments, a number is 1. In some embodiments, a number is 2. In some embodiments, a number is 3. In some embodiments, a number is 4. In some embodiments, a number is 5.

[00458] In some embodiments, low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a second subdomain independently comprise a 2'-F modification. In some embodiments, each sugar in a second subdomain independently contains no 2'-F modification. In some embodiments, each sugar in a second subdomain independently contains no 2'-F.

[00459] In some embodiments, sugars of opposite nucleosides to target adenosines ("opposite sugars"), sugars of nucleosides 5'-next to opposite nucleosides ("5'-next sugars"), and/or sugars of nucleosides 3'-next to opposite nucleosides ("3-next sugars") are independently and optionally 2'-F modified sugars, sugars comprising two 2'-H (e.g., natural DNA sugars), or sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, an opposite sugar is a 2'-F modified sugar. In some embodiments, an opposite sugar is a sugar comprising two 2'-H. In some embodiments, an opposite sugar is a natural DNA sugar. In some embodiments, an opposite sugar is a sugar comprising 2'-OH. In some embodiments, an opposite sugar is a natural RNA sugar. For example, in some embodiments, each of a 5'-next sugar, an opposite sugar and a 3'-next sugar in an oligonucleotide is independently a natural DNA sugar. In some embodiments, a 5'-next sugar is a 2'-F modified sugar, and each of an opposite sugar and a 3'-next sugar is independently a natural DNA sugar.

[00460] In some embodiments, a 5'-next sugar is a 2'-F modified sugar. In some embodiments, a 5'-next sugar is a sugar comprising two 2'-H. In some embodiments, a 5'-next sugar is a natural DNA sugar. In some embodiments, a 5'-next sugar is a sugar comprising 2'-OH. In some embodiments, a 5'-next sugar is a natural RNA sugar.

[00461] In some embodiments, a 3'-next sugar is a 2'-F modified sugar. In some embodiments, a 3'-next sugar is a sugar comprising two 2'-H. In some embodiments, a 3'-next sugar is a natural DNA sugar. In some embodiments, a 3'-next sugar is a sugar comprising 2'-OH. In some embodiments, a 3'-next sugar is a natural RNA sugar.

[00462] In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a second subdomain comprises 2'-MOE. In some embodiments, no more than about 50% of sugars in a second subdomain comprises 2'-MOE. In some embodiments, no sugars in a second subdomain comprises 2'-MOE.

[00463] In some embodiments, a second subdomain comprise about 1-10 (e.g., about 1-5, 1-4, 1-3, about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a second subdomain are modified internucleotidic linkages. In some embodiments, each internucleotidic linkage in a second subdomain is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PS internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PN internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a neutral internucleotidic linkage, e.g., n001. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, at least about 1-10 (e.g., about 1-5, 1-4, 1-3, about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) chiral internucleotidic linkages in a second subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a second subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a second subdomain is chirally controlled. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-10 (e.g., about 1-5, 1-4, 1-3, about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) chiral internucleotidic linkages in a second subdomain is *Sp*. In some embodiments, at least about 1-10 (e.g., about

1-5, 1-4, 1-3, about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) phosphorothioate internucleotidic linkages in a second subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a second subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a second subdomain is *Sp*. In some embodiments, the number is one or more. In some embodiments, the number is 2 or more. In some embodiments, the number is 3 or more. In some embodiments, the number is 4 or more. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, each internucleotidic linkage linking two second subdomain nucleosides is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage of a second subdomain is bonded to two nucleosides of the second subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a second subdomain and a nucleoside in a first or third subdomain may be properly considered an internucleotidic linkage of a second subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a second subdomain and a nucleoside in a first or third subdomain is a modified internucleotidic linkage; in some embodiments, it is a chiral internucleotidic linkage; in some embodiments, it is chirally controlled; in some embodiments, it is *Rp*; in some embodiments, it is *Sp*.

[00464] In some embodiments, a second subdomain comprises a certain level of *R*p internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in a second subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in a second subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in a second subdomain. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, 1-10 (e.g., about 1-5, 1-4, 1-3, about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages are independently *R*p chiral internucleotidic linkages. In some embodiments, the number is about or no more than about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the number is about or no more than about 3. In some embodiments, the number is about or no more than about

4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10. In some embodiments, a second subdomain comprise a higher level (in number and/or percentage) of *R*p internucleotidic linkage compared to other portions (e.g., a first domain, a second domain overall, a first subdomain, a third subdomain, or portions thereof). In some embodiments, a second subdomain comprise a higher level (in number and/or percentage) of *R*p internucleotidic linkage than *S*p internucleotidic linkage.

[00465] In some embodiments, each phosphorothioate internucleotidic linkage in a second subdomain is independently chirally controlled. In some embodiments, each is independently *S*p or *R*p. In some embodiments, a high level is *S*p as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a second subdomain is chirally controlled and is *S*p. In some embodiments, one or more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5) is *R*p.

[00466] In some embodiments, each internucleotidic linkage bonded to a natural DNA or RNA or 2'-F modified sugar in a second subdomain is independently a modified internucleotidic linkage as described herein. In some embodiments, each such modified internucleotidic linkage is independently a phosphorothioate or non-negatively charged internucleotidic linkage such as a phosphoryl guanidine internucleotidic linkage like n001. In some embodiments, each such modified internucleotidic linkage is independently a phosphorothioate or n001 internucleotidic linkage. In some embodiments, each internucleotidic linkage bonded to two second subdomain nucleosides is independently a phosphorothioate internucleotidic linkage. In some embodiments, each phosphorothioate internucleotidic linkage bonded to two second subdomain nucleosides is independently chirally controlled and is *S*p. In some embodiments, one or more internucleotidic linkages bonded to a second subdomain nucleoside are independently non-negatively charged internucleotidic linkages such as phosphoryl guanidine internucleotidic linkages like n001. In some embodiments, an internucleotidic linkage bonded to N_{-1} and N_{-2} is an non-negatively charged internucleotidic linkage. In some embodiments, it is a PN internucleotidic linkage. In some embodiments, it is a phosphoramidate internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is MsPA. In some embodiments, it is methylphosphonate. In some embodiments, it is chirally controlled and is *R*p. In some embodiments, it is chirally controlled and is *S*p. In some embodiments, N_{-1} comprises hypoxanthine and in some embodiments, is deoxyinosine. In some embodiments, a phosphoryl guanidine internucleotidic linkage such as n001 bonded to 3' position of a nucleoside comprising hypoxanthine is chirally controlled and is *S*p. In some embodiments, oligonucleotides comprising such *S*p phosphoryl guanidine internucleotidic linkages such as *S*p n001 bonded to 3' position of nucleosides comprising hypoxanthine (e.g., deoxyinosine) provide various benefits, e.g., higher activities, better properties, lower manufacturing cost, and/or more readily available manufacturing materials, etc.

[00467] In some embodiments, as illustrated in certain examples, a second subdomain comprises one or

more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Rp*. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Sp*. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in a second subdomain is about 1-5, or about 1, 2, 3, 4, or 5. In some embodiments, it is about 1. In some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in a second subdomain are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more (e.g., about 2, about 3, about 4 etc.) consecutive non-negatively charged internucleotidic linkages, are at the 3'-end of a second subdomain. In some embodiments, the last two or three or four internucleotidic linkages of a second subdomain comprise at least one internucleotidic linkage that is not a non-negatively charged internucleotidic linkage. In some embodiments, the last two or three or four internucleotidic linkages of a second subdomain comprise at least one internucleotidic linkage that is not n001. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second subdomain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second subdomain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a second subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second subdomain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second subdomain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a second subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last

nucleoside of a second subdomain and the first nucleoside of a third subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last nucleoside of a second subdomain and the first nucleoside of a third subdomain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last nucleoside of a second subdomain and the first nucleoside of a third subdomain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last nucleoside of a second subdomain and the first nucleoside of a third subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last nucleoside of a second subdomain and the first nucleoside of a third subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage such as n001.

[00468] In some embodiments, a second subdomain comprises one or more PO internucleotidic linkages. In some embodiments, a second subdomain comprises one or more natural phosphate linkages. In some embodiments, a second subdomain contains no PO internucleotidic linkages. In some embodiments, a second subdomain contains no natural phosphate linkages. In some embodiments, a second subdomain comprises at least 1 natural phosphate linkage. In some embodiments, a second subdomain comprises at least 2 natural phosphate linkages. In some embodiments, a second subdomain comprises at least 3 natural phosphate linkages. In some embodiments, a second subdomain comprises at least 4 natural phosphate linkages. In some embodiments, a second subdomain comprises at least 5 natural phosphate linkages.

[00469] In some embodiments, an opposite nucleoside is connected to its 5' immediate nucleoside through a natural phosphate linkage. In some embodiments, an opposite nucleoside is connected to its 5' immediate nucleoside through a natural phosphate linkage. In some embodiments, an opposite nucleoside is connected to its 5' immediate nucleoside through a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral charged internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled. In some embodiments, a chiral internucleotidic linkage is *Rp*. In some embodiments, a chiral internucleotidic linkage is *Sp*.

[00470] In some embodiments, an opposite nucleoside is connected to its 3' immediate nucleoside (-1 position relative to the opposite nucleoside) through a natural phosphate linkage. In some embodiments, an opposite nucleoside is connected to its 3' immediate nucleoside through a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral charged internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled. In some embodiments, a chiral

internucleotidic linkage is *Rp*. In some embodiments, a chiral internucleotidic linkage is *Sp*. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *Sp*. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *Rp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *Rp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *Sp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is not chirally controlled.

[00471] In some embodiments, a nucleoside at -1 position relative to an opposite nucleoside and a nucleoside at -2 position relative to an opposite nucleoside (e.g., in 5'-...$N_0N_{-1}N_{-2}$...3', if N_0 is an opposite nucleoside, N_{-1} is at -1 position and N_{-2} is at -2 position) is linked through a natural phosphate linkage. In some embodiments, they are connected through a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral charged internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled. In some embodiments, a chiral internucleotidic linkage is *Rp*. In some embodiments, a chiral internucleotidic linkage is *Sp*. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *Sp*. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *Rp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *Rp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *Sp*. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is not chirally controlled.

[00472] In some embodiments, a nucleoside of a second subdomain and a nucleoside of a third subdomain is linked through a natural phosphate linkage. In some embodiments, they are connected through a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral charged

internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled. In some embodiments, a chiral internucleotidic linkage is *R*p. In some embodiments, a chiral internucleotidic linkage is *S*p. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *S*p. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage and is *R*p. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *R*p. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is chirally controlled and is *S*p. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage (e.g., n001) and is not chirally controlled.

[00473] In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}$-3', wherein each of N_1, N_0, and N_{-1} is independently a nucleoside, N_1 and N_0 bond to an internucleotidic linkage as described herein, and N_{-1} and N_0 bond to an internucleotidic linkage as described herein, and N_0 is opposite to a target adenosine. In some embodiments, the sugar of each of N_1, N_0, and N_{-1} is independently a natural DNA sugar or a 2'-F modified sugar. In some embodiments, the sugar of each of N_1, N_0, and N_{-1} is independently a natural DNA sugar. In some embodiments, the sugar of N_1 is a 2'-modified sugar, and the sugar of each of N_0 and N_{-1} is independently a natural DNA sugar. In some embodiments, such oligonucleotides provide high editing levels. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently *R*p. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently an *R*p phosphorothioate internucleotidic linkage. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently an *R*p phosphorothioate internucleotidic linkage, and each other phosphorothioate internucleotidic linkage in an oligonucleotide, if any, is independently *S*p. In some embodiments, a 5' internucleotidic linkage bonded to N_1 is *R*p. In some embodiments, an internucleotidic linkage bonded to N_1 and N_0 (i.e., a 3' internucleotidic linkage bonded to N_1) is *R*p. In some embodiments, an internucleotidic linkage bonded to N_{-1} and N_0 is *R*p. In some embodiments, a 3' internucleotidic linkage bonded to N_{-1} is *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 or N_1 is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 or N_{-1} is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_1 is independently *R*p. In some embodiments, each *R*p internucleotidic linkage is independently an *R*p phosphorothioate internucleotidic linkage. In some embodiments, each other chirally controlled phosphorothioate internucleotidic linkage in an oligonucleotide is independently *S*p.

[00474] In some embodiments, sugar of a 5' immediate nucleoside (e.g., N_1) is independently selected from a natural DNA sugar, a natural RNA sugar, and a 2'-F modified sugar (e.g., R^{2s} is −F). In some embodiments, sugar of an opposite nucleoside (e.g., N_0) is independently selected from a natural DNA sugar,

a natural RNA sugar, and a 2'-F modified sugar. In some embodiments, sugar of a 3' immediate nucleoside (e.g., N_{-1}) is independently selected from a natural DNA sugar, a natural RNA sugar, and a 2'-F modified sugar. In some embodiments, sugars of a 5' immediate nucleoside, an opposite nucleoside, and a 3' immediate nucleoside are each independently a natural DNA sugar. In some embodiments, sugars of a 5' immediate nucleoside, an opposite nucleoside, and a 3' immediate nucleoside are a natural DNA sugar, a natural RNA sugar, and natural DNA sugar, respectively. In some embodiments, sugars of a 5' immediate nucleoside, an opposite nucleoside, and a 3' immediate nucleoside are a 2'-F modified sugar, a natural RNA sugar, and natural DNA sugar, respectively.

[00475] In some embodiments, sugar of an opposite nucleoside is a natural RNA sugar. In some embodiments, such an opposite nucleoside is utilized with a 3' immediate I nucleoside (which is optionally complementary to a C in a target nucleic acid when aligned). In some embodiments, an internucleotidic linkage between the 3' immediate nucleoside (e.g., N_{-1}) and its 3' immediate nucleoside (e.g., N_{-2}) is a non-negatively charged internucleotidic linkage, e.g., n001. In some embodiments, it is stereorandom. In some embodiments, it is chirally controlled and is *Rp*. In some embodiments, it is chirally controlled and is *Sp*.

[00476] In some embodiments, an internucleotidic linkage that is bonded to a 3' immediate nucleoside (e.g., N_{-1}) and its 3' neighboring nucleoside (e.g., N_{-2} in 5'-$N_1N_0N_{-1}N_{-2}$-3') is a modified internucleotidic linkage. In some embodiments, it is a chiral internucleotidic linkage. In some embodiments, it is stereorandom. In some embodiments, it is a stereorandom phosphorothioate internucleotidic linkage. In some embodiments, it is a stereorandom non-negatively charged internucleotidic linkage. In some embodiments, it is stereorandom n001. In some embodiments, it is chirally controlled. In some embodiments, it is a *Rp* phosphorothioate internucleotidic linkage. In some embodiments, it is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, it is chirally controlled. In some embodiments, it is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, it is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001.

[00477] In some embodiments, N_{-1} is I. In some embodiments, I is utilized replacing G, e.g., when a target nucleic acid comprises 5'−CA−3' wherein A is a target adenosine. In some embodiments, 5'-$N_1N_0N_{-1}$−3'is 5'-N_1N_0I−3'. In some embodiments, N_0 is b001A, b002A, b003A, b008U, b001C, C, A, or U. In some embodiments, N_0 is b001A, b002A, b008U, b001C, C, or A. In some embodiments, N_0 is b001A, b002A, b008U, or b001C. In some embodiments, N_0 is b001A. In some embodiments, N_0 is b002A. In some embodiments, N_0 is b003A. In some embodiments, N_0 is b008U. In some embodiments, N_0 is b001C. In some embodiments, N_0 is A. In some embodiments, N_0 is U.

[00478] As demonstrated herein, in some embodiments provided oligonucleotides comprising certain nucleobases (e.g., b001A, b002A, b008U, C, A, etc.) opposite to target adenosines can among other things provide improved editing efficiency (e.g., compared to a reference nucleobase such as U). In some embodiments, an opposite nucleoside is linked to an I to its 3' side.

[00479] In some embodiments, a second subdomain comprises an editing region as described herein.

[00480] In some embodiments, a second subdomain comprises a 5'-end portion, e.g., one having a length of about 1-5, 1-3, or 1, 2, 3, 4, or 5 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases.

[00481] In some embodiments, a 5'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 5'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-5, 1-3, or 1, 2, 3, 4, or 5) of sugars in a 5'-end portion are independently modified sugars. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 5'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00482] In some embodiments, low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 5'-end portion independently comprise a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a 5'-end portion independently contains no 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $–CH_2–$. In some embodiments, each sugar in a 5'-end portion independently contains no 2'-OMe.

[00483] In some embodiments, a 5'-end portion comprises one or more 2'-F modified sugars.

[00484] In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 5'-end are independently 2'-F modified sugars, sugars comprising two 2'-H (e.g., natural DNA sugars), or sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 5'-end portion are independently 2'-F modified sugars, natural DNA sugars, or natural RNA sugars. In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 5'-end portion are independently 2'-F modified sugars and natural DNA sugars. In some embodiments, a level is 100%. In some embodiments, sugars of a 5'-end portion are selected from sugars having two 2'-H (e.g., natural DNA sugar) and 2'-F modified sugars. In some embodiments, a 5'-end portion comprise 1, 2, 3, 4 or 5 2'-F modified sugars. In some embodiments, a 5'-end portion comprise 1, 2, 3, 4 or 5 sugars comprising two 2'-H. In some

embodiments, a 5'-end portion comprise 1, 2, 3, 4 or 5 natural DNA sugars. In some embodiments, a 5'-end portion comprise 1, 2, 3, 4 or 5 sugars comprising 2'-OH. In some embodiments, a 5'-end portion comprise 1, 2, 3, 4 or 5 natural RNA sugars. In some embodiments, a number is 1. In some embodiments, a number is 2. In some embodiments, a number is 3. In some embodiments, a number is 4. In some embodiments, a number is 5.

[00485] In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are *R*p. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are *S*p. In some embodiments, each internucleotidic linkage of a 5'-end portion is *S*p.

[00486] In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are *R*p. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 5'-end portion are *R*p. In some embodiments, each internucleotidic linkage of a 5'-end portion is *R*p.

[00487] In some embodiments, a 5'-end portion comprises one or more (e.g., about 1, 2, 3, 4, or 5) mismatches as described herein. In some embodiments, a 5'-end portion comprises one or more (e.g., about 1, 2, 3, 4, or 5) wobbles as described herein. In some embodiments, a 5'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00488] In some embodiments, a 5'-end portion comprises a nucleoside 5' next to an opposite nucleoside. In some embodiments, a nucleoside 5' next to an opposite nucleoside comprise a nucleobase as described herein.

[00489] In some embodiments, a second subdomain comprises a 3'-end portion, e.g., one having a length of about 1-5, 1-3, or 1, 2, 3, 4, or 5 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases. In some embodiments, a second subdomain consists a 5'-end portion and a 3'-end portion.

[00490] In some embodiments, a 3'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 3'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-5, 1-3, or 1, 2, 3, 4, or 5) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00491] In some embodiments, low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 3'-end portion independently comprise a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a 3'-end portion independently contains no 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $–CH_2–$. In some embodiments, each sugar in a 3'-end portion independently contains no 2'-OMe.

[00492] In some embodiments, a 3'-end portion comprises one or more 2'-F modified sugars.

[00493] In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 3'-end are independently 2'-F modified sugars, sugars comprising two 2'-H (e.g., natural DNA sugars), or sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 3'-end portion are independently 2'-F modified sugars, natural DNA sugars, or natural RNA sugars. In some embodiments, a high level (e.g., about 60-100%, or about 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more, or 100%) or all sugars in a 3'-end portion are independently 2'-F modified sugars and natural DNA sugars. In some embodiments, a level is 100%. In some embodiments, sugars of a 3'-end portion are selected from sugars having two 2'-H (e.g., natural DNA sugar) and 2'-F modified sugars. In some embodiments, a 3'-end portion comprise 1, 2, 3, 4 or 5 2'-F modified sugars. In some embodiments, a 3'-end portion comprise 1, 2, 3, 4 or 5 sugars comprising two 2'-H. In some embodiments, a 3'-end portion comprise 1, 2, 3, 4 or 5 natural DNA sugars. In some embodiments, a 3'-end portion comprise 1, 2, 3, 4 or 5 sugars comprising 2'-OH. In some embodiments, a 3'-end portion comprise 1, 2, 3, 4 or 5 natural RNA sugars. In some embodiments, a number is 1. In some embodiments, a number is 2. In some embodiments, a number is 3. In some embodiments, a number is 4. In some embodiments, a number is 5.

[00494] In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are *R*p. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are *S*p. In some embodiments, each internucleotidic linkage of a 3'-end portion is *S*p.

[00495] In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are *R*p. In some embodiments, one or more (e.g., about 1, 2, 3, 4, or 5) internucleotidic linkages of a 3'-end portion are *R*p. In some embodiments, each internucleotidic linkage of a 3'-end portion is *R*p.

[00496] In some embodiments, a 3'-end portion comprises one or more (e.g., about 1, 2, 3, 4, or 5) mismatches as described herein. In some embodiments, a 3'-end portion comprises one or more (e.g., about 1, 2, 3, 4, or 5) wobbles as described herein. In some embodiments, a 3'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00497] In some embodiments, a 3'-end portion comprises a nucleoside 3' next to an opposite nucleoside. In some embodiments, a nucleoside 3' next to an opposite nucleoside comprise a nucleobase as described herein. In some embodiments, a nucleoside 3' next to an opposite nucleoside forms a wobble pair with a corresponding nucleoside in a target nucleic acid. In some embodiments, the nucleobase of a nucleoside 3' next to an opposite nucleoside is hypoxanthine; in some embodiments, it is a derivative of hypoxanthine.

[00498] In some embodiments, a second subdomain recruits, promotes or contribute to recruitment of, a protein such as an ADAR protein, e.g., ADAR1, ADAR2, etc. In some embodiments, a second subdomain recruits, or promotes or contribute to interactions with, a protein such as an ADAR protein. In some embodiments, a second subdomain contacts with a RNA binding domain (RBD) of ADAR. In some embodiments, a second subdomain contacts with a catalytic domain of ADAR which has a deaminase activity. In some embodiments, a second subdomain contact with a domain that has a deaminase activity of ADAR1. In some embodiments, a second subdomain contact with a domain that has a deaminase activity of ADAR2. In some embodiments, various nucleobases, sugars and/or internucleotidic linkages of a second subdomain

may interact with one or more residues of proteins, e.g., ADAR proteins.

Third Subdomains

[00499] As described herein, in some embodiment, an oligonucleotide comprises a first domain and a second domain from 5' to 3'. In some embodiments, a second domain comprises or consists of a first subdomain, a second subdomain, and a third subdomain from 5' to 3'. Certain embodiments of a third subdomain are described below as examples.

[00500] In some embodiments, a third subdomain has a length of about 1-50, 1-40, 1-30, 1-20 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases. In some embodiments, a third subdomain has a length of about 5-30 nucleobases. In some embodiments, a third subdomain has a length of about 10-30 nucleobases. In some embodiments, a third subdomain has a length of about 10-20 nucleobases. In some embodiments, a third subdomain has a length of about 5-15 nucleobases. In some embodiments, a third subdomain has a length of about 13-16 nucleobases. In some embodiments, a third subdomain has a length of about 6-12 nucleobases. In some embodiments, a third subdomain has a length of about 6-9 nucleobases. In some embodiments, a third subdomain has a length of about 1-10 nucleobases. In some embodiments, a third subdomain has a length of about 1-7 nucleobases. In some embodiments, a third subdomain has a length of 1 nucleobase. In some embodiments, a third subdomain has a length of 2 nucleobases. In some embodiments, a third subdomain has a length of 3 nucleobases. In some embodiments, a third subdomain has a length of 4 nucleobases. In some embodiments, a third subdomain has a length of 5 nucleobases. In some embodiments, a third subdomain has a length of 6 nucleobases. In some embodiments, a third subdomain has a length of 7 nucleobases. In some embodiments, a third subdomain has a length of 8 nucleobases. In some embodiments, a third subdomain has a length of 9 nucleobases. In some embodiments, a third subdomain has a length of 10 nucleobases. In some embodiments, a third subdomain has a length of 11 nucleobases. In some embodiments, a third subdomain has a length of 12 nucleobases. In some embodiments, a third subdomain has a length of 13 nucleobases. In some embodiments, a third subdomain has a length of 14 nucleobases. In some embodiments, a third subdomain has a length of 15 nucleobases. In some embodiments, a third subdomain is shorter than a first subdomain. In some embodiments, a third subdomain is shorter than a first domain. In some embodiments, a third subdomain comprises a 3'-end nucleobase of a second domain.

[00501] In some embodiments, a third subdomain is about, or at least about, 5-95%, 10%-90%, 20%-80%, 30%-70%, 40%-70%, 40%-60%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% of a second domain. In some embodiments, a percentage is about 30%-80%. In some embodiments, a percentage is about 30%-70%. In some embodiments, a percentage is about 40%-60%. In some embodiments, a percentage is about 20%. In some embodiments, a percentage is about 25%. In some embodiments, a percentage is about 30%. In some embodiments, a percentage is about 35%. In some embodiments, a percentage is about 40%. In some embodiments, a percentage is about 45%. In some

embodiments, a percentage is about 50%. In some embodiments, a percentage is about 55%. In some embodiments, a percentage is about 60%. In some embodiments, a percentage is about 65%. In some embodiments, a percentage is about 70%. In some embodiments, a percentage is about 75%. In some embodiments, a percentage is about 80%. In some embodiments, a percentage is about 85%. In some embodiments, a percentage is about 90%. In some embodiments, the 5'-end nucleoside of a third subdomain is N_{-2}. In some embodiments, all nucleosides from N_{-2} to the 3'-end are in a third subdomain.

[00502] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches exist in a third subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 mismatch. In some embodiments, there are 2 mismatches. In some embodiments, there are 3 mismatches. In some embodiments, there are 4 mismatches. In some embodiments, there are 5 mismatches. In some embodiments, there are 6 mismatches. In some embodiments, there are 7 mismatches. In some embodiments, there are 8 mismatches. In some embodiments, there are 9 mismatches. In some embodiments, there are 10 mismatches.

[00503] In some embodiments, one or more (e.g., 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobbles exist in a third subdomain when an oligonucleotide is aligned with a target nucleic acid for complementarity. In some embodiments, there is 1 wobble. In some embodiments, there are 2 wobbles. In some embodiments, there are 3 wobbles. In some embodiments, there are 4 wobbles. In some embodiments, there are 5 wobbles. In some embodiments, there are 6 wobbles. In some embodiments, there are 7 wobbles. In some embodiments, there are 8 wobbles. In some embodiments, there are 9 wobbles. In some embodiments, there are 10 wobbles.

[00504] In some embodiments, duplexes of oligonucleotides and target nucleic acids in a third subdomain region comprise one or more bulges each of which independently comprise one or more mismatches that are not wobbles. In some embodiments, there are 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges. In some embodiments, the number is 0. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5.

[00505] In some embodiments, a third subdomain is fully complementary to a target nucleic acid.

[00506] In some embodiments, a third subdomain comprises one or more modified nucleobases.

[00507] In some embodiments, a third subdomain comprises a nucleoside opposite to a target adenosine (an opposite nucleoside). In some embodiments, a third subdomain comprises a nucleoside 3' next to an opposite nucleoside. In some embodiments, a third subdomain comprises a nucleoside 5' next to an opposite nucleoside. Various suitable opposite nucleosides, including sugars and nucleobases thereof, have been described herein.

[00508] In some embodiments, a third subdomain comprise a nucleoside opposite to a target adenosine, e.g., when the oligonucleotide forms a duplex with a target nucleic acid. Suitable nucleobases including modified nucleobases in opposite nucleosides are described herein. For example, in some embodiment, an

opposite nucleobase is optionally substituted or protected nucleobase selected from C, a tautomer of C, U, a tautomer of U, A, a tautomer of A, and a nucleobase which is or comprises Ring BA having the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA.

[00509] In some embodiments, a third subdomain comprises one or more sugars comprising two 2'-H (e.g., natural DNA sugars). In some embodiments, a third subdomain comprises one or more sugars comprising 2'-OH (e.g., natural RNA sugars). In some embodiments, a third subdomain comprises one or more modified sugars. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, a modified sugar is an acyclic sugar (e.g., by breaking a C2-C3 bond of a corresponding cyclic sugar).

[00510] In some embodiments, a third subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars. In some embodiments, a third subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently bicyclic sugars (e.g., a LNA sugar) or a 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a third subdomain comprises about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars which are independently 2'-OR modified sugars, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, the number is 1. In some embodiments, the number is 2. In some embodiments, the number is 3. In some embodiments, the number is 4. In some embodiments, the number is 5. In some embodiments, the number is 6. In some embodiments, the number is 7. In some embodiments, the number is 8. In some embodiments, the number is 9. In some embodiments, the number is 10. In some embodiments, the number is 11. In some embodiments, the number is 12. In some embodiments, the number is 13. In some embodiments, the number is 14. In some embodiments, the number is 15. In some embodiments, the number is 16. In some embodiments, the number is 17. In some embodiments, the number is 18. In some embodiments, the number is 19. In some embodiments, the number is 20. In some embodiments, R is methyl.

[00511] In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) sugars comprising 2'-OH. In some embodiments, a third

subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) sugars comprising two 2'-H. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) RNA sugars. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) DNA sugars.

[00512] In some embodiments, about 5%-100%, (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a third subdomain are independently a modified sugar. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a third subdomain are independently a bicyclic sugar (e.g., a LNA sugar) or a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all sugars in a third subdomain are independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, R is methyl. In some embodiments, N_{-2} comprises a 2'-OR modified sugar wherein R is not −H. In some embodiments, N_{-3} comprises a 2'-F modified sugar. In some embodiments, each nucleoside after N_{-3} independently comprises a 2'-OR modified sugar wherein R is not −H. In some embodiments, N_{-3} comprises a 2'-F modified sugar and each other nucleosides in a third subdomain independently comprises a 2'-OR modified sugar wherein R is not −H. In some embodiments, a 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar. In some

embodiments, 2'-OR modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe modified sugar.

[00513] In some embodiments, a third subdomain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently with a modification that is not 2'-F. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a third subdomain are independently modified sugars with a modification that is not 2'-F. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a third subdomain are independently modified sugars with a modification that is not 2'-F. In some embodiments, modified sugars of a third subdomain are each independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00514] In some embodiments, a third subdomain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%,

or 100%, etc.) of sugars in a third subdomain are independently modified sugars selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a third subdomain are independently modified sugars selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00515] In some embodiments, each sugar in a third subdomain independently comprises a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a third subdomain independently comprises a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification, wherein L^B is optionally substituted $–CH_2–$. In some embodiments, each sugar in a third subdomain independently comprises 2'-OMe.

[00516] In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) 2'-F modified sugars. In some embodiments, a third subdomain comprises no 2'-F modified sugars. In some embodiments, a third subdomain comprises one or more bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H. In some embodiments, levels of bicyclic sugars and/or 2'-OR modified sugars wherein R is not –H, individually or combined, are relatively high compared to level of 2'-F modified sugars. In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a third subdomain comprises 2'-F. In some embodiments, no more than about 50% of sugars in a third subdomain comprises 2'-F. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-$N(R)_2$ modification. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-NH_2 modification. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) bicyclic sugars, e.g., LNA sugars. In some embodiments, a third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

[00517] In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in a third subdomain comprises 2'-MOE. In some embodiments, no more than about 50% of sugars in a third subdomain comprises 2'-MOE. In some embodiments, no sugars in a third subdomain comprises 2'-MOE.

[00518] In some embodiments, a third subdomain comprise about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in a third subdomain are modified internucleotidic linkages. In some embodiments, each internucleotidic linkage in a third subdomain is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PS internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a PN internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified or chiral internucleotidic linkage is a neutral internucleotidic linkage, e.g., n001. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a third subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a third subdomain is chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%,

85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a third subdomain is chirally controlled. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in a third subdomain is *Sp*. In some embodiments, each is independently chirally controlled. In some embodiments, at least about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) phosphorothioate internucleotidic linkages in a third subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in a third subdomain is *Sp*. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of phosphorothioate internucleotidic linkages in a third subdomain is *Sp*. In some embodiments, the number is one or more. In some embodiments, the number is 2 or more. In some embodiments, the number is 3 or more. In some embodiments, the number is 4 or more. In some embodiments, the number is 5 or more. In some embodiments, the number is 6 or more. In some embodiments, the number is 7 or more. In some embodiments, the number is 8 or more. In some embodiments, the number is 9 or more. In some embodiments, the number is 10 or more. In some embodiments, the number is 11 or more. In some embodiments, the number is 12 or more. In some embodiments, the number is 13 or more. In some embodiments, the number is 14 or more. In some embodiments, the number is 15 or more. In some embodiments, a percentage is at least about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments,

each internucleotidic linkage linking two third subdomain nucleosides is independently a modified internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* chiral internucleotidic linkage. In some embodiments, each modified internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, each chiral internucleotidic linkages is independently a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage of a third subdomain is bonded to two nucleosides of the third subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a third subdomain and a nucleoside in a second subdomain may be properly considered an internucleotidic linkage of a third subdomain. In some embodiments, an internucleotidic linkage bonded to a nucleoside in a third subdomain and a nucleoside in a second subdomain is a modified internucleotidic linkage; in some embodiments, it is a chiral internucleotidic linkage; in some embodiments, it is chirally controlled; in some embodiments, it is *Rp*; in some embodiments, it is *Sp*.

[00519] In some embodiments, a third subdomain comprises a certain level of *Rp* internucleotidic linkages. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all internucleotidic linkages in a third subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chiral internucleotidic linkages in a third subdomain. In some embodiments, a level is about e.g., about 5%-100%, about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc. of all chirally controlled internucleotidic linkages in a third subdomain. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, a percentage is at least about 55%. In some embodiments, a percentage is at least about 60%. In some embodiments, a

percentage is at least about 65%. In some embodiments, a percentage is at least about 70%. In some embodiments, a percentage is at least about 75%. In some embodiments, a percentage is at least about 80%. In some embodiments, a percentage is at least about 85%. In some embodiments, a percentage is at least about 90%. In some embodiments, a percentage is at least about 95%. In some embodiments, a percentage is about 100%. In some embodiments, a percentage is about or no more than about 5%. In some embodiments, a percentage is about or no more than about 10%. In some embodiments, a percentage is about or no more than about 15%. In some embodiments, a percentage is about or no more than about 20%. In some embodiments, a percentage is about or no more than about 25%. In some embodiments, a percentage is about or no more than about 30%. In some embodiments, a percentage is about or no more than about 35%. In some embodiments, a percentage is about or no more than about 40%. In some embodiments, a percentage is about or no more than about 45%. In some embodiments, a percentage is about or no more than about 50%. In some embodiments, about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 1-5, e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 internucleotidic linkages are independently *Rp* chiral internucleotidic linkages. In some embodiments, the number is about or no more than about 1. In some embodiments, the number is about or no more than about 2. In some embodiments, the number is about or no more than about 3. In some embodiments, the number is about or no more than about 4. In some embodiments, the number is about or no more than about 5. In some embodiments, the number is about or no more than about 6. In some embodiments, the number is about or no more than about 7. In some embodiments, the number is about or no more than about 8. In some embodiments, the number is about or no more than about 9. In some embodiments, the number is about or no more than about 10.

[00520] In some embodiments, each phosphorothioate internucleotidic linkage in a third subdomain is independently chirally controlled. In some embodiments, each is independently *Sp* or *Rp*. In some embodiments, a high level is *Sp* as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in a third subdomain is chirally controlled and is *Sp*. In some embodiments, one or more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5) is *Rp*.

[00521] In some embodiments, as illustrated in certain examples, a third subdomain comprises one or more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Rp*. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *Sp*. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in a third subdomain is about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, it is about 1. In

some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in a third subdomain are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more (e.g., about 2, about 3, about 4 etc.) consecutive non-negatively charged internucleotidic linkages, are at the 3'-end of a third subdomain. In some embodiments, the last two or three or four internucleotidic linkages of a third subdomain comprise at least one internucleotidic linkage that is not a non-negatively charged internucleotidic linkage. In some embodiments, the last two or three or four internucleotidic linkages of a third subdomain comprise at least one internucleotidic linkage that is not n001. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a third subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a third subdomain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a third subdomain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a third subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of a third subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the last two nucleosides of a third subdomain are the last two nucleosides of a second domain. In some embodiments, the last two nucleosides of a third subdomain are the last two nucleosides of an oligonucleotide. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a third subdomain is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a third subdomain is a *Sp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a third subdomain is a *Rp* non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a third subdomain is a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of a third subdomain is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage such as n001. In some embodiments, it is chirally controlled and is *Rp*. In some embodiments, the last and/or the second last internucleotidic linkage of an oligonucleotide is a non-negatively charged internucleotidic linkage such as a phosphoryl guanidine internucleotidic linkage like n001. In some embodiments, it is chirally controlled and is *Rp*.

[00522] In some embodiments, a third subdomain comprises one or more (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) PO internucleotidic linkages. In some embodiments, a third subdomain comprises one or more (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10) natural phosphate linkages. In some embodiments, a third subdomain contains no natural phosphate linkages. In some embodiments, a third subdomain contains no natural phosphate

linkages. In some embodiments, the internucleotidic linkage bonded to N_{-2} and N_{-3} is a natural phosphate linkage. In some embodiments, sugar of N_{-3} is a 2'-F modified sugar and sugar of N_{-2} is a 2'-OR modified sugar wherein R is not −H (e.g., a 2'-OMe modified sugar). In some embodiments, among all internucleotidic linkages bonded to two nucleosides of a third subdomain, one is a natural phosphate linkage (e.g., between N_{-2} and N_{-3} as described herein), one is a *Rp* non-negatively charged internucleotidic linkage such as a phosphoryl guanidine internucleotidic linkage n001 (e.g., the last or the second last internucleotidic linkage of an oligonucleotide), and all the others are *Sp* phosphorothioate internucleotidic linkages.

[00523] In some embodiments, a third subdomain comprises a 5'-end portion, e.g., one having a length of about 1-20, 1-15, 1-10, 1-8, 1-5, 1-3, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleobases. In some embodiments, a 5'-end portion has a length of about 1-3 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases. In some embodiments, a length is 6 nucleobases. In some embodiments, a length is 7 nucleobases. In some embodiments, a length is 8 nucleobases. In some embodiments, a length is 9 nucleobases. In some embodiments, a length is 10 nucleobases. In some embodiments, a 5'-end portion comprises the 5'-end nucleobase of a third subdomain. In some embodiments, a third subdomain comprises or consists of a 3'-end portion and a 5'-end portion. In some embodiments, a 5'-end portion comprises the 5'-end nucleobase of a third subdomain. In some embodiments, a 5'-end portion of a third subdomain is bonded to a second subdomain.

[00524] In some embodiments, a 5'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 5'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-20, 1-15, 1-10, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 5'-end portion are independently modified sugars. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 5'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00525] In some embodiments, one or more of the modified sugars independently comprises 2'-F or 2'-OR, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, one or more of the modified sugars are independently 2'-F or 2'-OMe. In some embodiments, each modified sugar in a 5'-

end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 5'-end portion is independently a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl.

[00526] In some embodiments, compared to a 3'-end portion, 5' end portion contains a higher level (in numbers and/or percentage) of 2'-F modified sugars and/or sugars comprising two 2'-H (e.g., natural DNA sugars), and/or a lower level (in numbers and/or percentage) of other types of modified sugars, e.g., bicyclic sugars and/or sugars with 2'-OR modifications wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 3'-end portion, a 5'-end portion contains a higher level of 2'-F modified sugars and/or a lower level of 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 3'-end portion, a 5'-end portion contains a higher level of 2'-F modified sugars and/or a lower level of 2'-OMe modified sugars. In some embodiments, compared to a 3'-end portion, a 5'-end portion contains a higher level of natural DNA sugars and/or a lower level of 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, compared to a 3'-end portion, a 5'-end portion contains a higher level of natural DNA sugars and/or a lower level of 2'-OMe modified sugars. In some embodiments, a 5'-end portion contains low levels (e.g., no more than 50%, 40%, 30%, 25%, 20%, or 10%, or no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of modified sugars which are bicyclic sugars or sugars comprising 2'-OR wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl). In some embodiments, a 5'-end portion contains no modified sugars which are bicyclic sugars or sugars comprising 2'-OR wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl).

[00527] In some embodiments, one or more modified sugars independently comprise 2'-F. In some embodiments, no modified sugars comprises 2'-OMe or other 2'-OR modifications wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar of a 5'-end portion independently comprises two 2'-H or a 2'-F modification. In some embodiments, a 5'-end portion comprises 1, 2, 3, 4, or 5 2'-F modified sugars. In some embodiments, a 5'-end portion comprises 1-3 2'-F modified sugars. In some embodiments, a 5'-end portion comprises 1, 2, 3, 4, or 5 natural DNA sugars. In some embodiments, a 5'-end portion comprises 1-3 natural DNA sugars.

[00528] In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are *R*p. In some embodiments, one

or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 5'-end portion are *Sp*. In some embodiments, each internucleotidic linkage of a 5'-end portion is *Sp*. In some embodiments, a 5'-end portion contains a higher level (in number and/or percentage) of *Rp* internucleotidic linkage and/or natural phosphate linkage compared to a 3'-end portion.

[00529] In some embodiments, a 5'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) mismatches as described herein. In some embodiments, a 5'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) wobbles as described herein. In some embodiments, a 5'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00530] In some embodiments, a third subdomain comprises a 3'-end portion, e.g., one having a length of about 1-20, 1-15, 1-10, 1-8, 1-4, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleobases. In some embodiments, a 3'-end portion has a length of about 3-6 nucleobases. In some embodiments, a length is one nucleobase. In some embodiments, a length is 2 nucleobases. In some embodiments, a length is 3 nucleobases. In some embodiments, a length is 4 nucleobases. In some embodiments, a length is 5 nucleobases. In some embodiments, a length is 6 nucleobases. In some embodiments, a length is 7 nucleobases. In some embodiments, a length is 8 nucleobases. In some embodiments, a length is 9 nucleobases. In some embodiments, a length is 10 nucleobases. In some embodiments, a 3'-end portion comprises the 3'-end nucleobase of a third subdomain.

[00531] In some embodiments, a 3'-end portion comprises one or more sugars having two 2'-H (e.g., natural DNA sugars). In some embodiments, a 3'-end portion comprises one or more sugars having 2'-OH (e.g., natural RNA sugars). In some embodiments, one or more (e.g., about 1-20, 1-15, 1-10, 3-8, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in a 3'-end portion are independently modified sugars. In some embodiments, each sugar is independently a modified sugar. In some embodiments, modified sugars are independently selected from a bicyclic sugar (e.g., a LNA sugar), an acyclic sugar (e.g., a UNA sugar), a sugar with a 2'-OR modification, or a sugar with a 2'-$N(R)_2$ modification, wherein each R is independently optionally substituted C_{1-6} aliphatic.

[00532] In some embodiments, one or more of the modified sugars independently comprises 2'-F or 2'-

OR, wherein R is independently optionally substituted C_{1-6} aliphatic. In some embodiments, one or more of the modified sugars are independently 2'-F or 2'-OMe. In some embodiments, each modified sugar in a 3'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 3'-end portion is independently a bicyclic sugar (e.g., a LNA sugar) or a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar in a 3'-end portion is independently a sugar with a 2'-OR modification wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl.

[00533] In some embodiments, one or more sugars in a 3'-end portion independently comprise a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, each sugar in a 3'-end portion independently comprises a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic, or a 2'–O–L^B–4' modification. In some embodiments, L^B is optionally substituted $-CH_2-$. In some embodiments, L^B is $-CH_2-$. In some embodiments, each sugar in a 3'-end portion independently comprises 2'-OMe.

[00534] In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a modified internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a chiral internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are independently a chirally controlled internucleotidic linkage. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are *Rp*. In some embodiments, one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) internucleotidic linkages of a 3'-end portion are *Sp*. In some embodiments, each internucleotidic linkage of a 3'-end portion is *Sp*.

[00535] In some embodiments, a 3'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) mismatches as described herein. In some embodiments, a 3'-end portion comprises one or more (e.g., about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) wobbles as described herein. In some embodiments, a 3'-end portion is about 60-100% (e.g., 66%, 70%, 75%, 80%, 85%, 90%, 95%, or more) complementary to a target nucleic acid. In some embodiments, a complementarity is 60% or more. In some embodiments, a complementarity is 70% or more. In some embodiments, a complementarity is 75% or more. In some embodiments, a complementarity is 80% or more. In some embodiments, a complementarity is 90% or more.

[00536] In some embodiments, a third subdomain recruits, promotes or contribute to recruitment of, a protein such as an ADAR protein, e.g., ADAR1, ADAR2, etc. In some embodiments, a third subdomain recruits, or promotes or contribute to interactions with, a protein such as an ADAR protein. In some embodiments, a third subdomain contacts with a RNA binding domain (RBD) of ADAR. In some embodiments, a third subdomain contacts with a catalytic domain of ADAR which has a deaminase activity.

In some embodiments, a third subdomain contact with a domain that has a deaminase activity of ADAR1. In some embodiments, a third subdomain contact with a domain that has a deaminase activity of ADAR2. In some embodiments, various nucleobases, sugars and/or internucleotidic linkages of a third subdomain may interact with one or more residues of proteins, e.g., ADAR proteins.

[00537] As demonstrated herein, chiral control of linkage phosphorus of chiral internucleotidic linkages can be utilized in oligonucleotides to provide various properties and/or activities. In some embodiments, a *R*p internucleotidic linkage (e.g., a *R*p phosphorothioate internucleotidic linkage), a *S*p internucleotidic linkage (e.g., a *R*p phosphorothioate internucleotidic linkage), or a non-chirally controlled internucleotidic linkage (e.g., a non-chirally controlled phosphorothioate internucleotidic linkage) is at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine ("+" is counting from the nucleoside toward the 5'-end of an oligonucleotide with the internucleotidic linkage at the +1 position being the internucleotidic linkage between a nucleoside opposite to a target adenosine and its 5' side neighboring nucleoside (e.g., being the internucleotidic linkage bonded to the 5'-carbon of a nucleoside opposite to a target adenosine, or being between N_1 and N_0 of 5'-$N_1N_0N_{-1}$-3', wherein as described herein N_0 is the nucleoside opposite to a target adenosine), and "-" is counting from the nucleoside toward the 3'-end of an oligonucleotide with the internucleotidic linkage at the -1 position being the internucleotidic linkage between a nucleoside opposite to a target adenosine and its 3' side neighboring nucleoside (e.g., being the internucleotidic linkage bonded to the 3'-carbon of a nucleoside opposite to a target adenosine, or being between N_{-1} and N_0 of 5'-$N_1N_0N_{-1}$-3', wherein as described herein N_0 is the nucleoside opposite to a target adenosine)). In some embodiments, a *R*p internucleotidic linkage (e.g., a *R*p phosphorothioate internucleotidic linkage) is at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a *R*p internucleotidic linkage (e.g., a *R*p phosphorothioate internucleotidic linkage) is at one or more of positions -2, -1, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a *S*p internucleotidic linkage (e.g., a *S*p phosphorothioate internucleotidic linkage) is at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a *S*p internucleotidic linkage (e.g., a *S*p phosphorothioate internucleotidic linkage) is at one or more of positions -2, -1, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a non-chirally controlled internucleotidic linkage (e.g., a non-chirally controlled phosphorothioate internucleotidic linkage) is at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a non-chirally controlled internucleotidic linkage (e.g., a non-chirally controlled phosphorothioate internucleotidic linkage) is at one or more of positions -2, -1, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine.

[00538] In some embodiments, Rp is at position +8. In some embodiments, Rp is at position +7. In some embodiments, Rp is at position −6. In some embodiments, Rp is at position +5. In some embodiments, Rp is at position +4. In some embodiments, Rp is at position +3. In some embodiments, Rp is at position +2. In

some embodiments, Rp is at position +1. In some embodiments, Rp is at position -1. In some embodiments, Rp is at position -2. In some embodiments, Rp is at position -3. In some embodiments, Rp is at position -4. In some embodiments, Rp is at position -5. In some embodiments, Rp is at position -6. In some embodiments, Rp is at position -7. In some embodiments, Rp is at position -8. In some embodiments, Rp is the configuration of a chirally controlled phosphorothioate internucleotidic linkage. In some embodiments, Sp is at position +8. In some embodiments, Sp is at position +7. In some embodiments, Sp is at position −6. In some embodiments, Sp is at position +5. In some embodiments, Sp is at position +4. In some embodiments, Sp is at position +3. In some embodiments, Sp is at position +2. In some embodiments, Sp is at position +1. In some embodiments, Sp is at position -1. In some embodiments, Sp is at position -2. In some embodiments, Sp is at position -3. In some embodiments, Sp is at position -4. In some embodiments, Sp is at position -5. In some embodiments, Sp is at position -6. In some embodiments, Sp is at position -7. In some embodiments, Sp is at position -8. In some embodiments, Sp is the configuration of a chirally controlled phosphorothioate internucleotidic linkage. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +8. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +7. In some embodiments, a non-chirally controlled internucleotidic linkage is at position −6. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +5. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +4. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +3. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +2. In some embodiments, a non-chirally controlled internucleotidic linkage is at position +1. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -1. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -2. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -3. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -4. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -5. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -6. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -7. In some embodiments, a non-chirally controlled internucleotidic linkage is at position -8. In some embodiments, a non-chirally controlled internucleotidic linkage is a non-chirally controlled phosphorothioate internucleotidic linkage.

[00539] In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Rp* internucleotidic linkages (e.g., *Rp* phosphorothioate internucleotidic linkages). In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Sp* internucleotidic linkages (e.g., *Sp* phosphorothioate internucleotidic linkages). In some embodiments, a first domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled internucleotidic linkages (e.g., non-chirally controlled phosphorothioate internucleotidic linkages). In some embodiments, such internucleotidic linkages are consecutive. In some embodiments, at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all of internucleotidic linkages in a first domain are chirally controlled and are *Sp*. In some embodiments, at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all of phosphorothioate

internucleotidic linkages in a first domain are chirally controlled and are *Sp*. In some embodiments, a second domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Rp* internucleotidic linkages (e.g., *Rp* phosphorothioate internucleotidic linkages). In some embodiments, a second domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Sp* internucleotidic linkages (e.g., *Sp* phosphorothioate internucleotidic linkages). In some embodiments, a second domain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled internucleotidic linkages (e.g., non-chirally controlled phosphorothioate internucleotidic linkages). In some embodiments, such internucleotidic linkages are consecutive. In some embodiments, at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all of internucleotidic linkages in a second domain are chirally controlled and are *Sp*. In some embodiments, at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all of phosphorothioate internucleotidic linkages in a second domain are chirally controlled and are *Sp*. In some embodiments, a first subdomain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Rp* internucleotidic linkages (e.g., *Rp* phosphorothioate internucleotidic linkages). In some embodiments, a first subdomain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) *Sp* internucleotidic linkages (e.g., *Sp* phosphorothioate internucleotidic linkages). In some embodiments, a first subdomain comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled internucleotidic linkages (e.g., non-chirally controlled phosphorothioate internucleotidic linkages). In some embodiments, such internucleotidic linkages are consecutive. In some embodiments, such internucleotidic linkages are at 3'-end portion of a first subdomain.

[00540] In some embodiments, one or more natural phosphate linkages are utilized in provided oligonucleotides and compositions thereof. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise one or more (e.g., about, or at least about, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, or more) natural phosphate linkages. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise two or more (e.g., about, or at least about, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, or more) consecutive natural phosphate linkages. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than about, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 natural phosphate linkages. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 consecutive natural phosphate linkages. In some embodiments, about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all internucleotidic linkages in provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains,

etc.) are natural phosphate linkages. In some embodiments, about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all internucleotidic linkages in provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) are not natural phosphate linkages. In some embodiments, about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all internucleotidic linkages in provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) are not consecutive natural phosphate linkages.

[00541] In some embodiments, provided oligonucleotides or portions thereof comprises one or more natural phosphate linkages and one or more modified internucleotidic linkages. In some embodiments, provided oligonucleotides or portions thereof comprises one or more natural phosphate linkages and one or more chirally controlled modified internucleotidic linkages. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than about, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 natural phosphate linkages each of which independently bonds to two sugars comprising no 2'-OR modification, wherein R is as described herein but not −H. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 consecutive natural phosphate linkages each of which independently bonds to two sugars comprising no 2'-OR modification, wherein R is as described herein but not −H. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than about, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 natural phosphate linkages each of which independently bonds to two 2'-F modified sugars. In some embodiments, provided oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) comprise no more than 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50 consecutive natural phosphate linkages each of which independently bonds to two 2'-F modified sugars. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, e.g., no more than 2, no more than 3, no more than 4, no more than 5, etc., internucleotidic linkages that bond to two sugars comprising no 2'-OR modification wherein R is as described herein but not −H are natural phosphate linkages. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, e.g., no

more than 2, no more than 3, no more than 4, no more than 5, etc., internucleotidic linkages that bond to two 2'-F modified sugars are natural phosphate linkages. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., no more than 10%, no more than 15%, no more than 20%, no more than 25%, no more than about 30%, no more than about 40%, no more than 50% etc., of internucleotidic linkages that bond to two sugars comprising no 2'-OR modification wherein R is as described herein but not −H are natural phosphate linkages. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, e.g., no more than 10%, no more than 15%, no more than 20%, no more than 25%, no more than about 30%, no more than about 40%, no more than 50% etc., of internucleotidic linkages that bond to two 2'-F modified sugars are natural phosphate linkages. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, e.g., no more than 2, no more than 3, no more than 4, no more than 5, etc., consecutive internucleotidic linkages that bond to two sugars comprising no 2'-OR modification wherein R is as described herein but not −H are natural phosphate linkages. In some embodiments, in oligonucleotides or portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, third subdomains, etc.) no more than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, or 50, e.g., no more than 2, no more than 3, no more than 4, no more than 5, etc., consecutive internucleotidic linkages that bond to two 2'-F modified sugars are natural phosphate linkages.

[00542] In some embodiments, a natural phosphate linkage is at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine. In some embodiments, a natural phosphate linkage is at one or more of positions -1 and +1. In some embodiments, a natural phosphate linkage is at positions -1 and +1. In some embodiments, a natural phosphate linkage is at position -1. In some embodiments, a natural phosphate linkage is at position +1. In some embodiments, a natural phosphate linkage is at position +8. In some embodiments, a natural phosphate linkage is at position +7. In some embodiments, a natural phosphate linkage is at position −6. In some embodiments, a natural phosphate linkage is at position +5. In some embodiments, a natural phosphate linkage is at position +4. In some embodiments, a natural phosphate linkage is at position +3. In some embodiments, a natural phosphate linkage is at position +2. In some embodiments, a natural phosphate linkage is at position -2. In some embodiments, a natural phosphate linkage is at position -3. In some embodiments, a natural phosphate linkage is at position -4. In some embodiments, a natural phosphate linkage is at position -5. In some embodiments, a natural phosphate linkage is at position -6. In some embodiments, a natural phosphate linkage is at position -7. In some embodiments, a natural phosphate linkage is at position -8. In some embodiments, a natural

phosphate linkage is at position -1, and a modified internucleotidic linkage is at position +1. In some embodiments, a natural phosphate linkage is at position +1, and a modified internucleotidic linkage is at position -1. In some embodiments, a modified internucleotidic linkage is chirally controlled. In some embodiments, a modified internucleotidic linkage is chirally controlled and is Sp. In some embodiments, a modified internucleotidic linkage is a chirally controlled Sp phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is chirally controlled and is Rp. In some embodiments, a modified internucleotidic linkage is a chirally controlled Rp phosphorothioate internucleotidic linkage. In some embodiments, a second domain comprises no more than 2 natural phosphate linkages. In some embodiments, a second domain comprises no more than 1 natural phosphate linkages. In some embodiments, a single natural phosphate linkage can be utilized at various positions of an oligonucleotide or a portion thereof (e.g., a first domain, a second domain, a first subdomain, a second subdomain, a third subdomain, etc.).

[00543] In some embodiments, particular types of sugars are utilized at particular positions of oligonucleotides or portions thereof. For example, in some embodiments, a first domain comprises a number of 2'-F modified sugars (and optionally a number of 2'-OR modified sugars wherein R is not–H, in some embodiments at lower levels than 2'-F modified sugars), a first subdomain comprises a number of 2'-OR modified sugars wherein R is not–H (e.g., 2'-OMe modified sugars; and optionally a number of 2'-F sugars, in some embodiments at lower levels than 2'-OR modified sugars wherein R is not –H), a second domain comprises one or more natural DNA sugars (no substitution at 2' position) and/or one or more 2'-F modified sugars, and/or a third subdomain comprises a number of 2'-OR modified sugars wherein R is not–H (e.g., 2'-OMe modified sugars; and optionally a number of 2'-F sugars, in some embodiments at lower levels than 2'-OR modified sugars wherein R is not –H). In some embodiments, particular type of sugars are independently at one or more of positions -8, -7, -6, -5, -4, -3, -2, -1, 0, +1, +2, +3, +4, +5, +6, +7, and +8 of a nucleoside opposite to a target adenosine ("+" is counting from the nucleoside toward the 5'-end of an oligonucleotide, "-" is counting from the nucleoside toward the 3'-end of an oligonucleotide, with position 0 being the position of the nucleoside opposite to a target adenosine, e.g.: 5'- … $N_{+2}N_{+1}N_0N_{-1}N_{-2}$….3'). As those skilled in the art reading the present disclosure will readily appreciate, numbering in the present disclosure may not include "+" in some instances, for example, N_{+2} may be referred to as N_2. In some embodiments, particular types of sugars are independently at one or more of positions -5, -4, -3, -2, -1, 0, +1, +2, +3, +4, and +5. In some embodiments, particular types of sugars are independently at one or more of positions -3, -2, -1, 0, +1, +2, and +3. In some embodiments, particular types of sugars are independently at one or more of positions -2, -1, 0, +1, and +2. In some embodiments, particular types of sugars are independently at one or more of positions -1, 0, and +1. In some embodiments, a particular type of sugar is at position +8. In some embodiments, a particular type of sugar is at position +7. In some embodiments, a particular type of sugar is at position +6. In some embodiments, a particular type of sugar is at position +5. In some embodiments, a particular type of sugar is at position +4. In some embodiments, a particular type of sugar is at position +3. In some embodiments, a particular type of sugar is at position +2. In some embodiments, a particular type of sugar is at position +1. In

some embodiments, a particular type of sugar is at position 0. In some embodiments, a particular type of sugar is at position -8. In some embodiments, a particular type of sugar is at position -7. In some embodiments, a particular type of sugar is at position -6. In some embodiments, a particular type of sugar is at position -5. In some embodiments, a particular type of sugar is at position -4. In some embodiments, a particular type of sugar is at position -3. In some embodiments, a particular type of sugar is at position -2. In some embodiments, a particular type of sugar is at position -1. In some embodiments, a particular type of sugar is independently a sugar selected from a natural DNA sugar (two 2'-H at 2'-carbon), a 2'-OMe modified sugar, and a 2'-F modified sugar. In some embodiments, a particular type of sugar is independently a sugar selected from a natural DNA sugar (two 2'-H at 2'-carbon) and a 2'-OMe modified sugar. In some embodiments, a particular type of sugar is independently a sugar selected from a natural DNA sugar (two 2'-H at 2'-carbon) and a 2'-F modified sugar, e.g., for sugars at position 0, -1, and/or +1. In some embodiments, a particularly type of sugar is a natural DNA sugar (two 2'-H at 2'-carbon), e.g., at position -1, 0 or +1. In some embodiments, a particular type of sugar is 2'-F modified sugar, e.g., at position -8, -7, -6, -5, -4, -3, -2, -1, 0, +1, +2, +3, +4, +5, +6, +7, and/or +8. In some embodiments, a particular type of sugar is 2'-F modified sugar, e.g., at position -8, -7, -6, -5, -4, -3, -2, +2, +3, +4, +5, +6, +7, and/or +8. In some embodiments, a 2'-F modified sugar is at position -2. In some embodiments, a 2'-F modified sugar is at position -3. In some embodiments, a 2'-F modified sugar is at position -4. In some embodiments, a 2'-F modified sugar is at position +2. In some embodiments, a 2'-F modified sugar is at position +3. In some embodiments, a 2'-F modified sugar is at position +4. In some embodiments, a 2'-F modified sugar is at position +5. In some embodiments, a 2'-F modified sugar is at position +6. In some embodiments, a 2'-F modified sugar is at position +7. In some embodiments, a 2'-F modified sugar is at position +8. In some embodiments, a particular type of sugar is 2'-OMe modified sugar, e.g., at position -8, -7, -6, -5, -4, -3, -2, -1, 0, +1, +2, +3, +4, +5, +6, +7, and/or +8. In some embodiments, a particular type of sugar is 2'-OMe modified sugar, e.g., at position -8, -7, -6, -5, -4, -3, -2, +2, +3, +4, +5, +6, +7, and/or +8. In some embodiments, a 2'-OMe modified sugar is at position -2. In some embodiments, a 2'-OMe modified sugar is at position -3. In some embodiments, a 2'-OMe modified sugar is at position -4. In some embodiments, a 2'-OMe modified sugar is at position +2. In some embodiments, a 2'-OMe modified sugar is at position +3. In some embodiments, a 2'-OMe modified sugar is at position +4. In some embodiments, a 2'-OMe modified sugar is at position +5. In some embodiments, a 2'-OMe modified sugar is at position +6. In some embodiments, a 2'-OMe modified sugar is at position +7. In some embodiments, a 2'-OMe modified sugar is at position +8. In some embodiments, a sugar at position 0 is not a 2'-MOE modified sugar. In some embodiments, a sugar at position 0 is a natural DNA sugar (two 2'-H at 2'-carbon). In some embodiments, a sugar at position 0 is not a 2'-MOE modified sugar. In some embodiments, a sugar at position -1 is not a 2'-MOE modified sugar. In some embodiments, a sugar at position -2 is not a 2'-MOE modified sugar. In some embodiments, a sugar at position -3 is not a 2'-MOE modified sugar. In some embodiments, a first domain comprises one or more 2'-F modified sugars, and optionally 2'-OR modified sugars (in some embodiments at lower levels than 2'-F modified sugars) wherein R is as described herein and is not −H. In

some embodiments, a first domain comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-OR modified sugars (in some embodiments at lower levels that 2'-F modified sugars) wherein R is as described herein and is not –H. In some embodiments, a first domain comprise 1, 2, 3, or 4, or 1 and no more than 1, 2 and no more than 2, 3 and no more than 3, or 4 and no more than 4 2'-OR modified sugars wherein R is C_{1-6} aliphatic. In some embodiments, the first, second, third and/or fourth sugars of a first domain are independently 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, sugars comprising 2'-OR are consecutive. In some embodiments, a first domain comprises 2, 3, 4, 5, 6, 7, 8, 9, or 10 consecutive sugars at its 5'-end, wherein each sugar independently comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, 2'-OR is 2'-OMe. In some embodiments, 2'-OR is 2'-MOE. In some embodiments, a second domain comprises one or more 2'-OR modified sugars (in some embodiments at lower levels) wherein R is as described herein and is not –H, and optionally 2'-F modified sugars (in some embodiments at lower levels). In some embodiments, a first subdomain comprises one or more 2'-OR modified sugars (in some embodiments at lower levels) wherein R is as described herein and is not –H, and optionally 2'-F modified sugars (in some embodiments at lower levels). In some embodiments, a third subdomain comprises one or more 2'-OR modified sugars (in some embodiments at lower levels) wherein R is as described herein and is not –H, and optionally 2'-F modified sugars (in some embodiments, at lower levels; in some embodiments, at higher levels). In some embodiments, a third subdomain comprises about, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 2'-F modified sugars. In some embodiments, a third subdomain comprises about, or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 consecutive 2'-F modified sugars. In some embodiments, about or at least about, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% of sugars in a third subdomain independently comprise 2'-F modification. In some embodiments, the first 2'-F modified sugar in the third subdomain (from 5' to 3') is not the first sugar in the third subdomain. In some embodiments, the first 2'-F modified sugar in the third subdomain is at position -3 relative to the nucleoside opposition to a target adenosine. In some embodiments, each sugar in a third subdomain is independently a modified sugar. In some embodiments, each sugar in a third subdomain is independently a modified sugar, wherein the modification is selected from 2'-F and 2'-OR, wherein R is C_{1-6} aliphatic. In some embodiments, a modification in selected from 2'-F and 2'-OMe. In some embodiments, each modified sugar in a third subdomain is independently 2'-F modified sugar. In some embodiments, each modified sugar in a third subdomain is independently 2'-OMe modified sugar. In some embodiments, one or more modified sugars in a third subdomain are independently 2'-OMe modified sugar, and one or more modified sugars in a third subdomain are independently 2'-F modified sugar. In some embodiments, each modified sugar in a third subdomain is independently a 2'-F modified sugar except the first sugar of a third subdomain, which in some embodiments is a 2'-OMe modified sugar. In some embodiments, a third subdomain comprises one or more 2'-OR modified sugars (in some embodiments at lower levels) wherein R is as described herein and is not –H, and optionally 2'-F modified sugars (in some embodiments at lower levels). In some embodiments, 2'-OR is 2'-OMe. In some embodiments, 2'-OR is 2'-MOE.

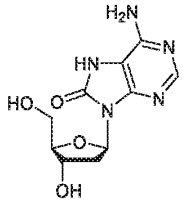
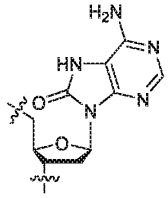
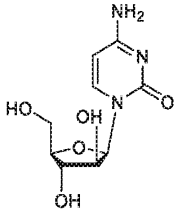
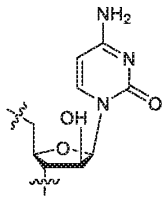
Editing Region

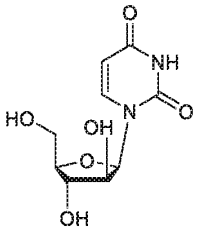
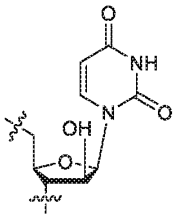
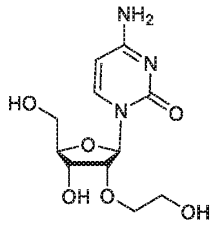
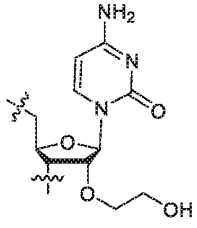
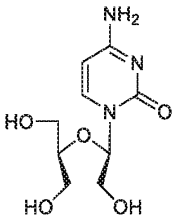
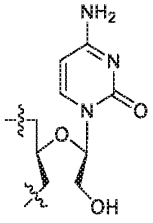
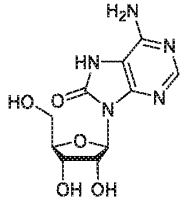
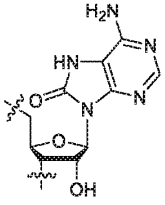
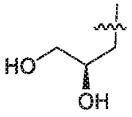
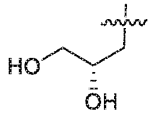
[00544] In some embodiments, the present disclosure provides oligonucleotides comprising editing regions, e.g., regions comprising or consisting of 5'-$N_1N_0N_{-1}$-3' as described herein. In some embodiments, an editing region is or comprises a nucleoside opposite to a target adenosine (typically, when base sequences of oligonucleotides are aligned with target sequences for maximal complementarity, and/or oligonucleotides hybridize with target nucleic acids) and its neighboring nucleosides. In some embodiments, an editing region is or comprises three nucleobases, wherein the nucleobase in the middle is a nucleoside opposite to a target adenosine. In some embodiments, a nucleoside opposite to a target adenosine is N_0 as described herein.

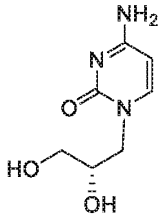
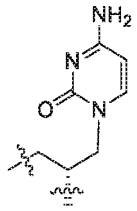
[00545] In some embodiments, the nucleobase of a nucleoside opposite to a target adenosine (may be referred to as BA_0) is C. In some embodiments, BA_0 is a modified nucleobase as described herein. In some embodiments, a nucleobase, e.g., BA_0, is or comprises Ring BA which has the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA, wherein the nucleobase is optionally substituted or protected. In some embodiments, a nucleobase is optionally substituted or protected, or optionally substituted or protected tautomer of C, T, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], and zdnp. In some embodiments, a nucleobase is optionally substituted or protected, or optionally substituted or protected tautomer of zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, or b001G. In some embodiments, the nucleobase of N_0 is optionally substituted or protected, or optionally substituted or protected tautomer of C, zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, or b001G, and the sugar of N_0 is a natural DNA sugar. In some embodiments, the nucleobase of N_0 is optionally substituted or protected, or optionally substituted or protected tautomer of C, zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, or b001G, and the sugar of N_0 is a natural RNA sugar. In some embodiments, the nucleobase of N_0 is optionally substituted or protected, or optionally substituted or protected tautomer of C, zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, or b001G, and the sugar of N_0 is a 2'-F modified sugar. In some embodiments, the nucleobase of N_0 is optionally substituted or protected, or optionally substituted or protected tautomer of C, zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C,

b003C, b002I, b003I, or b001G, and the sugar of N_0 is a bicyclic sugar (e.g., a LNA sugar, a cEt sugar, etc.). In some embodiments, the nucleobase of N_0 is optionally substituted or protected, or optionally substituted or protected tautomer of C, zdnp, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, or b001G, and the sugar of N_0 is a sugar comprising a 6-membered ring, e.g., sm19. In some embodiments, BA_0 is C. In some embodiments, BA_0 is T. In some embodiments, BA_0 is hypoxanthine. In some embodiments, BA_0 is U. In some embodiments, BA_0 is b001U. In some embodiments, BA_0 is b002U. In some embodiments, BA_0 is b003U. In some embodiments, BA_0 is b004U. In some embodiments, BA_0 is b005U. In some embodiments, BA_0 is b006U. In some embodiments, BA_0 is b007U. In some embodiments, BA_0 is b008U. In some embodiments, BA_0 is b009U. In some embodiments, BA_0 is b011U. In some embodiments, BA_0 is b012U. In some embodiments, BA_0 is b013U. In some embodiments, BA_0 is b014U. In some embodiments, BA_0 is b015U. In some embodiments, BA_0 is b001A. In some embodiments, BA_0 is b002A. In some embodiments, BA_0 is b003A. In some embodiments, BA_0 is b004A. In some embodiments, BA_0 is b005A. In some embodiments, BA_0 is b006A. In some embodiments, BA_0 is b007A. In some embodiments, BA_0 is b001C. In some embodiments, BA_0 is b002C. In some embodiments, BA_0 is b003C. In some embodiments, BA_0 is b004C. In some embodiments, BA_0 is b005C. In some embodiments, BA_0 is b006C. In some embodiments, BA_0 is b007C. In some embodiments, BA_0 is b008C. In some embodiments, BA_0 is b009C. In some embodiments, BA_0 is b002I. In some embodiments, BA_0 is b003I. In some embodiments, BA_0 is b004I. In some embodiments, BA_0 is b014I. In some embodiments, BA_0 is b001G. In some embodiments, BA_0 is b002G. In some embodiments, BA_0 is [3nT]. In some embodiments, BA_0 is [3ne5U]. In some embodiments, BA_0 is [3nflU]. In some embodiments, BA_0 is [3npry5U]. In some embodiments, BA_0 is [3ncn5U]. In some embodiments, BA_0 is [nathp6o8A]. In some embodiments, BA_0 is [ipr6o8A]. In some embodiments, BA_0 is [c7In]. In some embodiments, BA_0 is [c39z48In]. In some embodiments, BA_0 is [z2c3In]. In some embodiments, BA_0 is [z5C]. In some embodiments, sugar of N_0 is a natural DNA sugar, or a substituted natural DNA sugar one of whose 2'-H is substituted with –OH or –F and the other 2'-H is not substituted. In some embodiments, sugar of N_0 is a natural DNA sugar. In some embodiments, sugar of N_0 is deoxyribose. In some embodiments, sugar of N_0 is a natural RNA sugar. In some embodiments, sugar of N_0 is an acyclic sugar. In some embodiments, sugar of N_0 is sm01. In some embodiments, sugar of N_0 is sm04. In some embodiments, sugar of N_0 is sm11. In some embodiments, sugar of N_0 is sm12. In some embodiments, sugar of N_0 is rsm13. In some embodiments, sugar of N_0 is rsm14. In some embodiments, sugar of N_0 is sm15. In some embodiments, sugar of N_0 is sm16. In some embodiments, sugar of N_0 is sm17. In some embodiments, sugar of N_0 is sm18. In some embodiments, sugar of N_0 is sm19. In some embodiments, sugar of N_0 is a bicyclic sugar. In some embodiments, sugar of N_0 is a LNA sugar. In some embodiments, sugar of N_0 is a cEt sugar. In some embodiments, sugar of N_0 is a (S)-cEt sugar. Among other things, the present disclosure confirmed that various modified nucleobases and/or various sugars may be utilized at N_0 in oligonucleotides to provide adenosine-editing activities. In some embodiments, it was

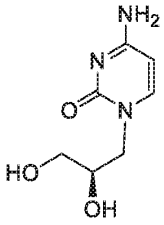
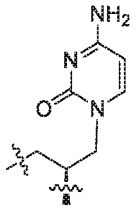
observed that b001A as BA_0 can provide improved adenosine editing efficiency compared to a reference nucleobase (e.g., under comparable conditions including in otherwise identical oligonucleotides, assessed in identical or comparable assays, etc.). In some embodiments, it was observed that b008U as BA_0 can provide improved adenosine editing efficiency. In some embodiments, a reference nucleobase is U. In some embodiments, a reference nucleobase is T. In some embodiments, a reference nucleobase is C. In some embodiments, it was observed that when sugar of N_0 comprises certain 6-membered ring, e.g., when sugar of N_0 is sm19, editing activity may be improved over a reference sugar, e.g., a natural DNA sugar. In some embodiments, it was observed that LNA sugars can be utilized in N_0 or neighboring nucleosides. In some embodiments, it was observed 2'-OR modified sugars wherein R is optionally substituted aliphatic, e.g., 2'-OMe, 2'-MOE, etc., can be in N_0 or neighboring nucleosides. As confirmed by various oligonucleotide compositions and assessments, technologies described in the present disclosure can provide, among other things, greater flexibility than other technologies with respect to sugars, nucleobases, linkages, etc., that can be utilized for editing including at N_0. For example, while various reports asserted that 2'-OMe modified sugar at N_0 blocked editing, various base modifications described herein, e.g., those of formula BA-III-e such as b008U, can be utilized with 2'-OMe modified sugar at N_0 to provide editing, in some cases with at least comparable levels compared to other sugars such as natural DNA sugar. In some embodiments, one or two or three sugars at N_{-1}, N_0 or N_{-1} are independently modified sugars. In some embodiments, a sugar at N_1 is a modified sugar. In some embodiments, a sugar at N_0 is a modified sugar. In some embodiments, a sugar at N_{-1} is a modified sugar. In some embodiments, sugars at N_1 and N_0 are each independently a modified sugar. In some embodiments, sugars at N_{-1} and N_0 are each independently a modified sugar. In some embodiments, sugars at N_1 and N_{-1} are each independently a modified sugar. In some embodiments, sugars at N_1, N_0 and N_{-1} are each independently a modified sugar. In some embodiments, a modified sugar is a 2'-modified sugar as described herein. In some embodiments, a modified sugar is a 2'-OR^{ak} modified sugar. In some embodiments, a modified sugar is a 2'-OMe modified sugar. In some embodiments, a modified sugar is a 2'-MOE modified sugar. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar. In some embodiments, an oligonucleotide comprises a nucleoside, e.g., N_0, the nucleobase of which is a modified nucleobase as described herein, and the sugar of which is a sugar as described herein. For example, in some embodiments, a nucleoside is b001A. In some embodiments, a nucleoside is b008U. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a natural DNA sugar. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-modified sugar. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-F modified sugar. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-OMe modified sugar. In some embodiments, the nucleobase of a nucleoside is b001A and the sugar is a 2'-MOE modified sugar. In some embodiments, the nucleobase of a nucleoside is [3nT] and

the sugar is a natural DNA sugar. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-modified sugar. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-F modified sugar. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-OMe modified sugar. In some embodiments, the nucleobase of a nucleoside is [3nT] and the sugar is a 2'-MOE modified sugar.In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a natural DNA sugar. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-modified sugar. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-F modified sugar. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-OMe modified sugar. In some embodiments, the nucleobase of a nucleoside is b008U and the sugar is a 2'-MOE modified sugar. In some embodiments, a nucleoside opposite to a target adenosine, e.g., N_0, is dC. In some embodiments, it is rC. In some embodiments, it is fC. In some embodiments, it is dT. In some embodiments, it is rT. In some embodiments, it is fT. In some embodiments, it is dU. In some embodiments, it is rU. In some embodiments, it is fU. In some embodiments, it is b001A (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Csm15 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Usm15 (which when utilized for a nucleoside

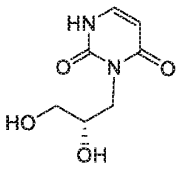
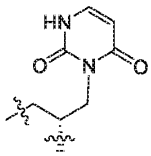
refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is rCsm13 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Csm04 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b001rA (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, a sugar is a (R)-GNA sugar . In some embodiments, a sugar is a (S)-GNA sugar . In some embodiments, it is S-GNA C, also referred herein as Csm11 (which when utilized

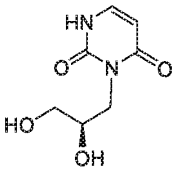
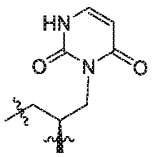
for a nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is R-GNA C, also referred herein as Csm12 (which when utilized for a

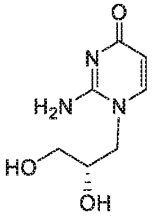
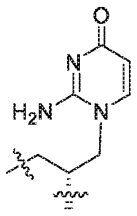
nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is S-GNA b008U, also referred herein as b008Usm11 (which when utilized for a

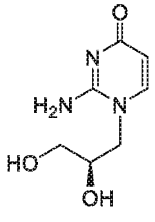
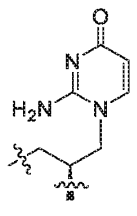
nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is R-GNA b008U, also referred herein as b008Usm12 (which when

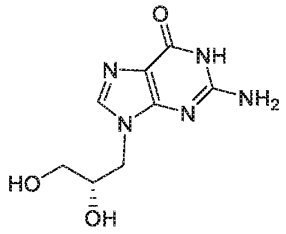
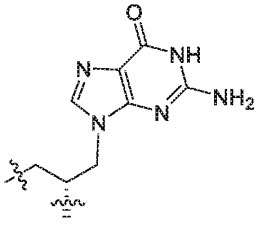
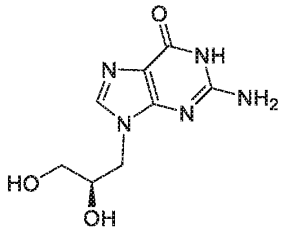
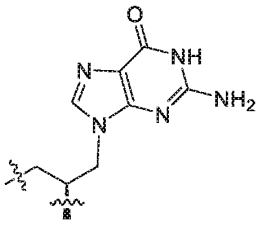
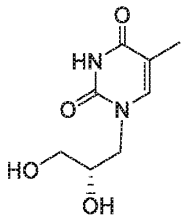
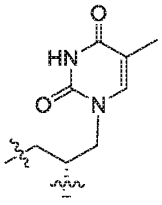
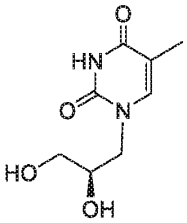
utilized for a nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is S-GNA isoC, also referred herein as b009Csm11 (which

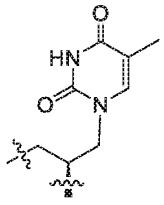



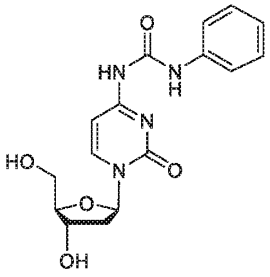
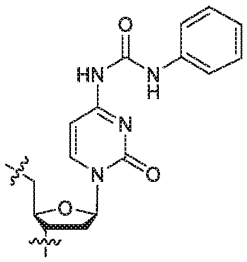
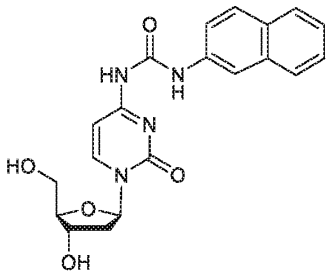
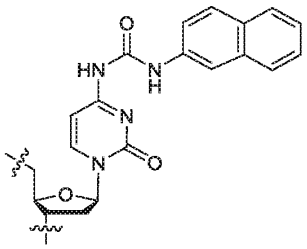
when utilized for a nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is R-GNA isoC, also referred herein as b009Csm12 (which

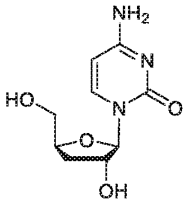
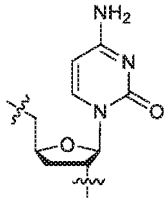



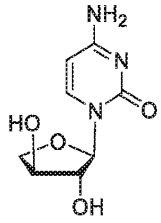
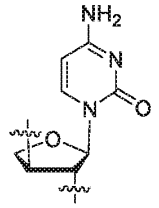
when utilized for a nucleoside refers to or in an oligonucleotide chain unless

specified otherwise). In some embodiments, it is S-GNA G, also referred herein as Gsm11 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is R-GNA G, also referred herein as Gsm12 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is S-GNA T, also referred herein as Tsm11 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is R-GNA T, also referred herein as Tsm12 (which when utilized for a nucleoside refers to  or

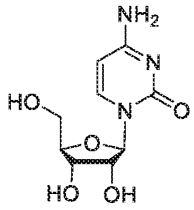
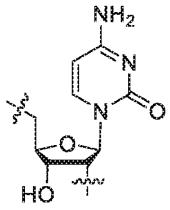


in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b004C (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b007C (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise).

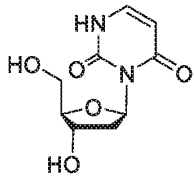
In some embodiments, it is Csm16 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Csm17

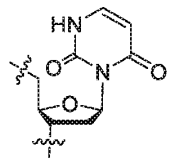
(which when utilized for a nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is rCsm14 (which when utilized for a nucleoside refers

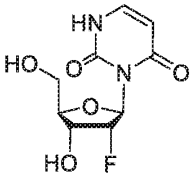
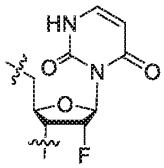
to or in an oligonucleotide chain unless specified otherwise). In some



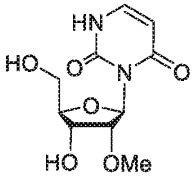
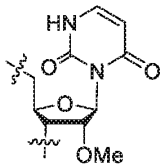
embodiments, it is b008U (which when utilized for a nucleoside refers to or



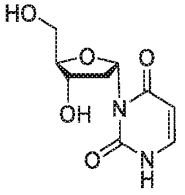
in an oligonucleotide chain unless specified otherwise). In some embodiments, it is fb008U

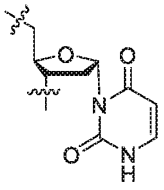
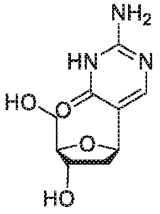
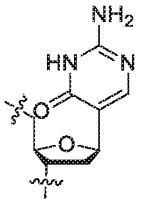
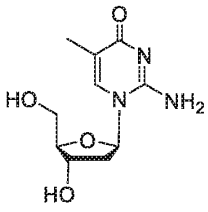
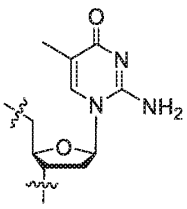
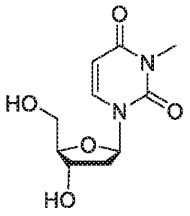
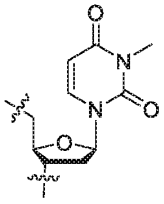
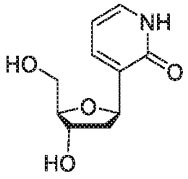
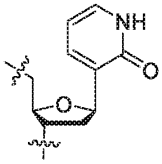
(which when utilized for a nucleoside refers to or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is mb008U (which when utilized for a nucleoside

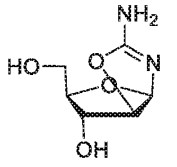



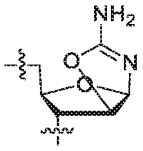
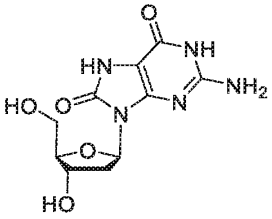
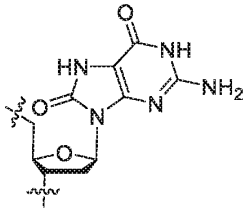
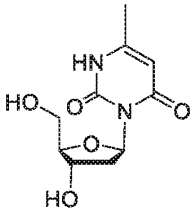
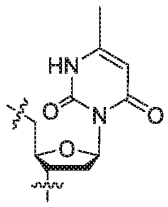
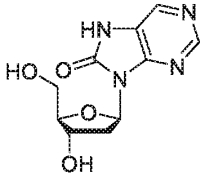
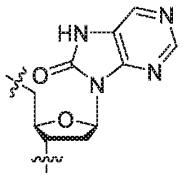
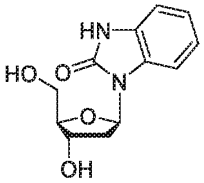
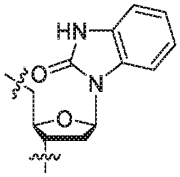
refers to or in an oligonucleotide chain unless specified otherwise). In

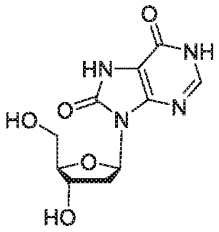
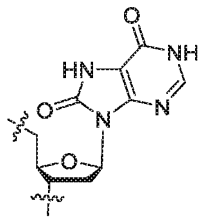
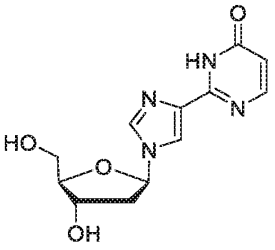
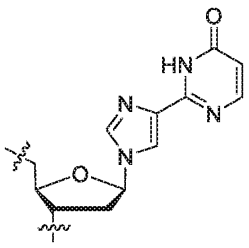
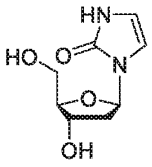
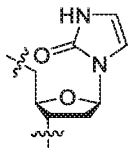
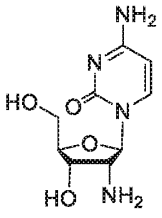
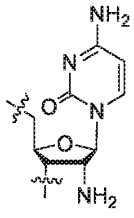
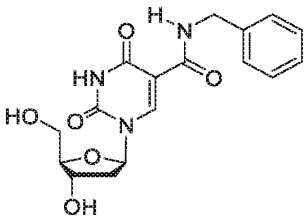
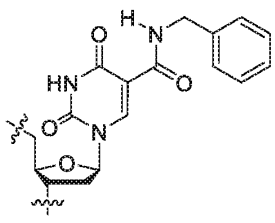
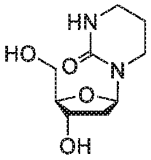
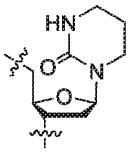


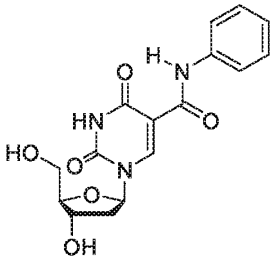
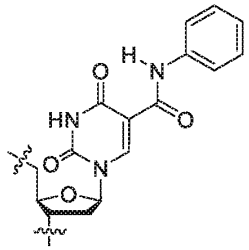
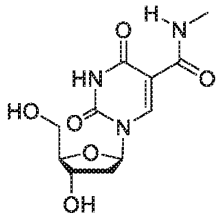
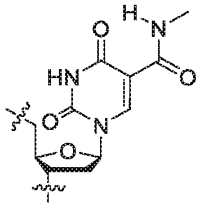
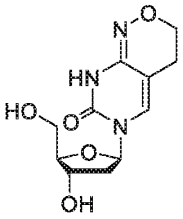
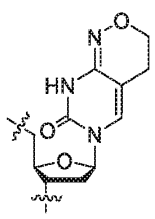
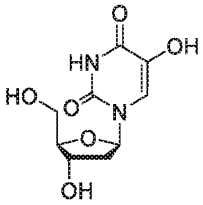
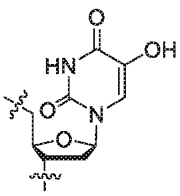
some embodiments, it is b010U (which when utilized for a nucleoside refers to or

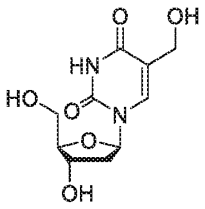
 in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b001C (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b008C (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b011U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b012U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is abasic. In some embodiments, it is L010. In



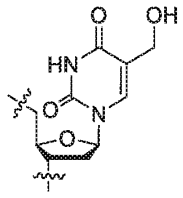
some embodiments, it is L034 (which when utilized for a nucleoside refers to  or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b002G (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b013U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b002A (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b003A (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b004l

(which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b014I (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b009U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is aC (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b001U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b002U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some

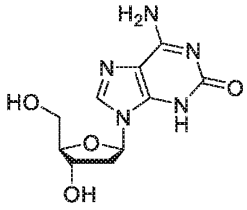
embodiments, it is b003U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b004U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b005U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b006U (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some



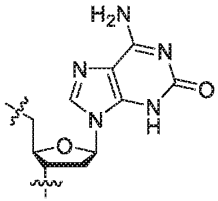
embodiments, it is b007U (which when utilized for a nucleoside refers to



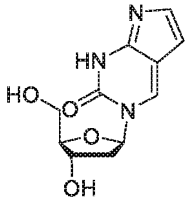
in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b001G



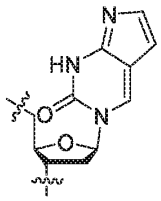
(which when utilized for a nucleoside refers to



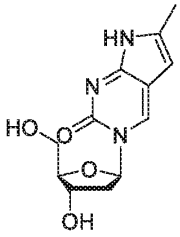
or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b002C (which when utilized for



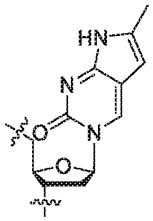
a nucleoside refers to



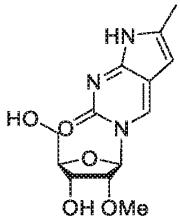
or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b003C (which when utilized for a nucleoside refers to



or

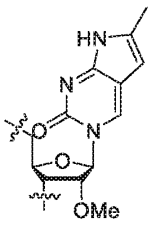


in an oligonucleotide chain unless specified otherwise). In some

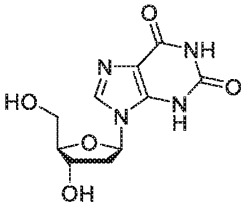


embodiments, it is b003mC (which when utilized for a nucleoside refers to

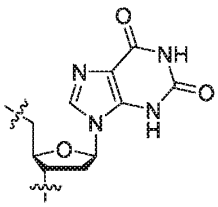
or



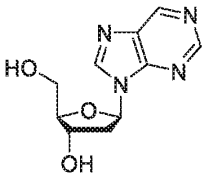
in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b002I



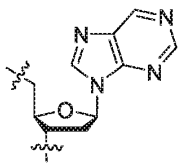
(which when utilized for a nucleoside refers to



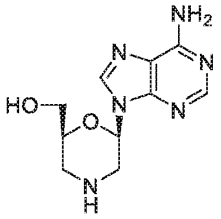
or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b003I (which when utilized for a nucleoside refers to



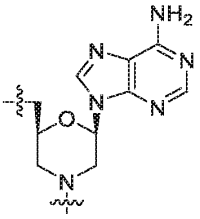
or



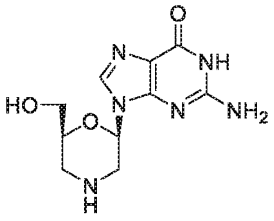
in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Asm01 (which when utilized for a nucleoside refers to



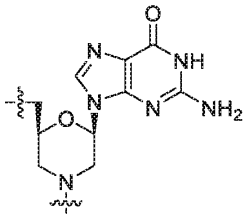
or



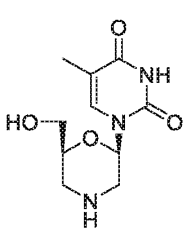
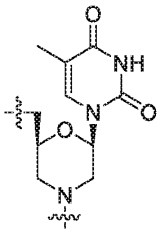
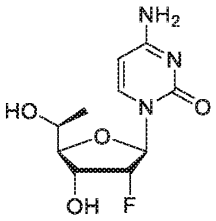
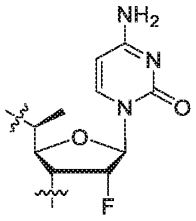
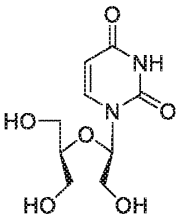
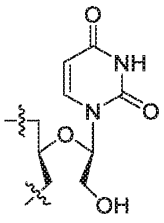
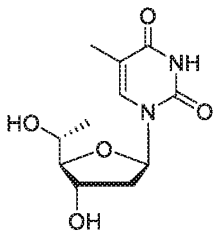
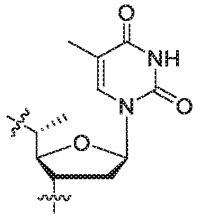
in an oligonucleotide chain unless specified otherwise; in some embodiments, the nitrogen atom is bonded to a linkage phosphorus). In some embodiments, it is Gsm01 (which when utilized for a nucleoside refers to

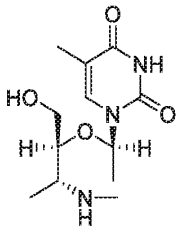
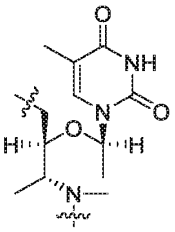


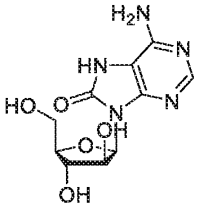
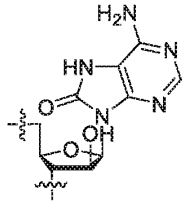
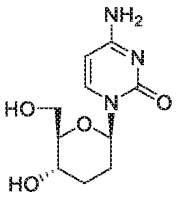
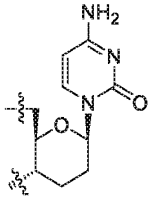
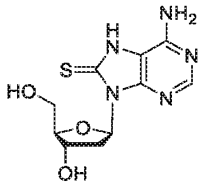
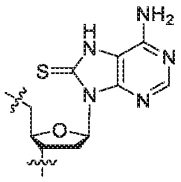
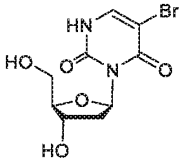
or

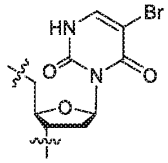


in an oligonucleotide chain unless specified otherwise; in some embodiments, the nitrogen atom is bonded to a linkage phosphorus). In some embodiments, it is Tsm01 (which when utilized for a nucleoside refers to

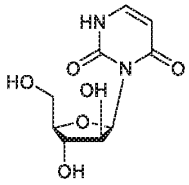
  or in an oligonucleotide chain unless specified otherwise; in some embodiments, the nitrogen atom is bonded to a linkage phosphorus). In some embodiments, it is 5MsfC (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Usm04 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is 5MRdT (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Tsm18

(which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise; in some embodiments, the nitrogen atom is bonded to a linkage phosphorus).

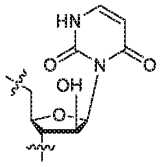
In some embodiments, it is b001Asm15 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is Csm19 (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b006A (which when utilized for a nucleoside refers to  or  in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b014U (which when utilized for a nucleoside refers to  or



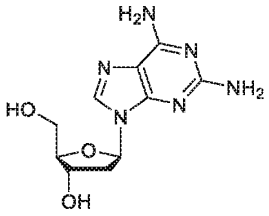
in an oligonucleotide chain unless specified otherwise). In some embodiments, it is



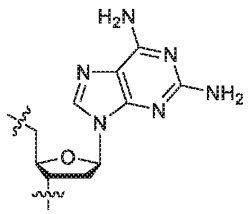
b008Usm15 (which when utilized for a nucleoside refers to



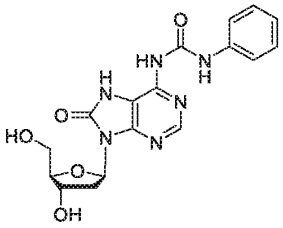
or in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b004A (which when utilized for a nucleoside refers to



or



in an oligonucleotide chain unless specified otherwise). In some embodiments, it is b005A (which when utilized for a nucleoside refers to



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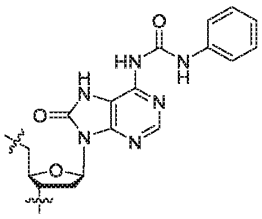
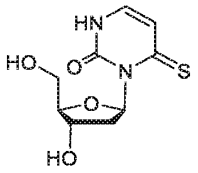


in an oligonucleotide chain unless specified otherwise).

In some embodiments, it is b015U (which when utilized for a nucleoside refers to



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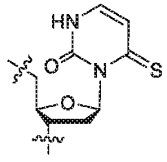


in an oligonucleotide chain unless specified otherwise). In some embodiments, N_0 is abasic. In some embodiments, N_0 is L010.

[00546] In some embodiments, as demonstrated in various examples, certain modified nucleosides or nucleobases, e.g., b001A, b008U etc., can provide improved editing, e.g., when compared to dC at positions opposite to target adenosines. In some embodiments, it was observed that certain nucleosides, e.g., dC, b001A,

b001rA, Csm15, b001C, etc. can provide improved adenosine editing efficiency when utilized at N_0 compared to a reference nucleoside (e.g., under comparable conditions including in otherwise identical oligonucleotides, assessed in identical or comparable assays, etc.). In some embodiments, N_0 is b001A. In some embodiments, N_0 is b001Asm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b002A. In some embodiments, N_0 is b003A. In some embodiments, N_0 is b004A. In some embodiments, N_0 is b005A. In some embodiments, N_0 is b006A. In some embodiments, N_0 is b004I. In some embodiments, N_0 is b014I. In some embodiments, N_0 is b002G. In some embodiments, N_0 is dC. In some embodiments, N_0 is b001C. In some embodiments, N_0 is b009U. In some embodiments, N_0 is b010U. In some embodiments, N_0 is b011U. In some embodiments, N_0 is b012U. In some embodiments, N_0 is b013U. In some embodiments, N_0 is b014U. In some embodiments, N_0 is b015U. In some embodiments, N_0 is [3nT]. In some embodiments, N_0 is b008Usm15. In some embodiments, N_0 is b008Usm19. In some embodiments, N_0 is Csm04. In some embodiments, N_0 is Csm11. In some embodiments, N_0 is Csm12. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is Csm19. In some embodiments, N_0 is b009Csm11. In some embodiments, N_0 is b009Csm12. In some embodiments, N_0 is Gsm11. In some embodiments, N_0 is Gsm12. In some embodiments, N_0 is Tsm11. In some embodiments, N_0 is Tsm12. In some embodiments, a reference nucleoside is rU. In some embodiments, a reference nucleoside is dU. In some embodiments, a reference nucleoside is dT. In some embodiments, at N_0 position there is no nucleobase. In some embodiments, at N_0 position it is L010. In some embodiments, sugar of N_0 is sm15.

[00547] In some embodiments, replacing guanine with hypoxanthine at position -1 (e.g., replacing dG with dI) can provide improved editing. Certain data are provided in figures and others as examples.

[00548] In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}$-3' wherein each of N_1, N_0, and N_{-1} is independently a nucleoside as described herein. In some embodiments, an oligonucleotide comprises 5'-$N_2N_1N_0N_{-1}N_{-2}$-3' wherein each of N_2, N_1, N_0, N_{-1}, and N_{-2} is independently a nucleoside as described herein. In some embodiments, an oligonucleotide comprises 5'-$N_3N_2N_1N_0N_{-1}N_{-2}N_{-3}$-3' wherein each of N_3, N_2, N_1, N_0, N_{-1}, N_{-2}, and N_{-3} is independently a nucleoside as described herein. In some embodiments, an oligonucleotide comprises 5'-$N_4N_3N_2N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}$-3' wherein each of N_4, N_3, N_2, N_1, N_0, N_{-1}, N_{-2}, N_{-3}, and N_{-4} is independently a nucleoside as described herein. In some embodiments, an oligonucleotide comprises 5'-$N_5N_4N_3N_2N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}$-3' wherein each of N_5, N_4, N_3, N_2, N_1, N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, and N_{-5} is independently a nucleoside as described herein. In some embodiments, an oligonucleotide comprises 5'-$N_6N_5N_4N_3N_2N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}N_{-6}$-3' wherein each of N_6, N_5, N_4, N_3, N_2, N_1, N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is independently a nucleoside as described herein. In some embodiments, N_n wherein n is a positive number, e.g., N_1, may also be referred to as N_{+1}. In some embodiments, such an oligonucleotide can form a duplex with a nucleic acid (e.g., a RNA nucleic acid) and can edit a target adenosine which is opposite to N_0. In some embodiments, N_{-6} is the last nucleoside of an oligonucleotide (counting from the 5'-end).

[00549] In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}N_{-2}$-3', wherein each of N_1, N_0, N_{-1}, and N_{-2} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}N_{-}$

$_2N_{-3}$-3', wherein each of N_1, N_0, N_{-1}, N_{-2}, and N_{-3} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}$-3', wherein each of N_1, N_0, N_{-1}, N_{-2}, N_{-3}, and N_{-4} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}$-3', wherein each of N_1, N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, and N_{-5} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}N_{-6}$-3', wherein each of N_1, N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is independently a nucleoside. Various sugars, nucleobases and internucleotidic linkages can be utilized for these nucleosides. For example, in some embodiments, sugar of N_1 is a natural DNA sugar. In some embodiments, sugar of N_1 is a 2'-F modified sugar. In some embodiments, sugar of N_1 is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, nucleobase of N_0 is BA_0 as described herein. In some embodiments, it is [dma6o8A]. In some embodiments, it is [3nU]. In some embodiments, it is zdnp. In some embodiments, sugar of N_0 is a natural DNA sugar. In some embodiments, sugar of N_0 is a 2'-F modified sugar. In some embodiments, sugar of N_0 is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, sugar of N_0 is a 2'-OMe modified sugar. In some embodiments, the internucleotidic linkage between N_1 and N_0 is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, sugar of N_{-1} is a natural DNA sugar. In some embodiments, nucleobase of N_{-1} is hypoxanthine. In some embodiments, the internucleotidic linkage between N_0 and N_{-1} is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, sugar of N_{-2} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, the internucleotidic linkage between N_{-1} and N_{-2} is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a natural phosphate linkage. In some embodiments, it is a PN internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, it is methylphosphonate. In some embodiments, sugar of N_{-3} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, the internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage. In some embodiments, sugar of N_{-4} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, the internucleotidic linkage between N_{-3} and N_{-4} is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, sugar of N_{-5} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar. In some embodiments, the internucleotidic linkage between N_{-4} and N_{-5} is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, sugar of N_{-6} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic, e.g., a 2'-OMe or 2'-MOE modified sugar.

In some embodiments, the internucleotidic linkage between N_{-5} and N_{-6} is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a PN internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an oligonucleotide comprises N_2 which is a nucleoside linked to N_1 by an internucleotidic linkage. In some embodiments, sugar of N_2 is a 2'-F modified sugar. In some embodiments, the internucleotidic linkage between N_2 and N_1 is a modified internucleotidic linkage, e.g., a phosphorothioate internucleotidic linkage. In some embodiments, a first domain is linked to N_2 by an internucleotidic linkage.

[00550] In some embodiments, sugar of N_1 is a 2'-deoxyribose (natural DNA sugar), 2'-F modified sugar, or a 2'-OR^{ak} modified sugar wherein R^{ak} is optionally substituted C_{1-6} aliphatic (e.g., a 2'-OMe modified sugar or a 2'-MOE modified sugar); the internucleotidic linkage between N_1 and N_0 is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_0 is a 2'-deoxyribose, 2'-F modified sugar, or a 2'-OR^{ak} modified sugar wherein R^{ak} is optionally substituted C_{1-6} aliphatic (e.g., a 2'-OMe modified sugar or a 2'-MOE modified sugar); the internucleotidic linkage between N_0 and N_{-1} is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_{-1} is a 2'-deoxyribose; the internucleotidic linkage between N_{-1} and N_{-2} is a PN internucleotidic linkage or a non-negatively charged internucleotidic linkage (e.g., a methylphosphonate internucleotidic linkage); sugar of N_{-2} is a 2'-OR^{ak} modified sugar wherein R^{ak} is optionally substituted C_{1-6} aliphatic (e.g., a 2'-OMe modified sugar or a 2'-MOE modified sugar); the internucleotidic linkage between N_{-2} and N_{-3} is a PO internucleotidic linkage (e.g., a natural phosphate linkage); and sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, sugar of N_1 is a 2'-deoxyribose; the internucleotidic linkage between N_1 and N_0 is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_0 is a 2'-deoxyribose; the internucleotidic linkage between N_0 and N_{-1} is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_{-1} is a 2'-deoxyribose; the internucleotidic linkage between N_{-1} and N_{-2} is a PN internucleotidic linkage or a non-negatively charged internucleotidic linkage (e.g., a methylphosphonate internucleotidic linkage); sugar of N_{-2} is a 2'-OMe modified sugar; the internucleotidic linkage between N_{-2} and N_{-3} is a PO internucleotidic linkage (e.g., a natural phosphate linkage); and sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, sugar of N_1 is a 2'-deoxyribose; the internucleotidic linkage between N_1 and N_0 is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_0 is a 2'-OMe modified sugar; the internucleotidic linkage between N_0 and N_{-1} is a PS internucleotidic linkage (e.g., a phosphorothioate internucleotidic linkage); sugar of N_{-1} is a 2'-deoxyribose; the internucleotidic linkage between N_{-1} and N_{-2} is a PN internucleotidic linkage or a non-negatively charged internucleotidic linkage (e.g., a methylphosphonate internucleotidic linkage); sugar of N_{-2} is a 2'-OMe modified sugar; the internucleotidic linkage between N_{-2} and N_{-3} is a PO internucleotidic linkage (e.g., a natural phosphate linkage); and sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, a PO internucleotidic linkage is a natural phosphate linkage. In some embodiments, a PS

internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a PS internucleotidic linkage is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_{-1} and N_{-2} is a PN internucleotidic linkage. In some embodiments, a PN internucleotidic linkage is a phosphoramidate internucleotidic linkage. In some embodiments, a PN internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a PN internucleotidic linkage is n001. In some embodiments, a PN internucleotidic linkage is MsPA. In some embodiments, a PN internucleotidic linkage is *Rp*. In some embodiments, the internucleotidic linkage between N_{-1} and N_{-2} is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is a methylphosphonate internucleotidic linkage. In some embodiments, sugar of N_1 is a 2'-deoxyribose, sugar of N_0 is a 2'-deoxyribose, sugar of N_{-1} is a 2'-deoxyribose, sugar of N_{-2} is a 2'-OMe modified sugar, and sugar of N_{-3} is a 2'-F modified sugar. In some embodiments, sugar of N_1 is a 2'-deoxyribose, sugar of N_0 is a 2'-OMe modified sugar, sugar of N_{-1} is a 2'-deoxyribose, sugar of N_{-2} is a 2'-OMe modified sugar, and sugar of N_{-3} is a 2'-F modified sugar.

[00551] As those skilled in the art reading the present disclosure will appreciate, various internucleotidic linkages can be utilized to connect nucleosides, e.g., neighboring nucleosides of N_6, N_5, N_4, N_3, N_2, N_1, N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6}. In some embodiments, a internucleotidic linkage is a phosphorothioate internucleotidic linkage, a natural phosphate linkage, a phosphoryl guanidine internucleotidic linkage (e.g., n001) or a methylphosphonate internucleotidic linkage.

[00552] In some embodiments, an oligonucleotide comprises 5'-$N_2N_1N_0N_{-1}N_{-2}$-3', wherein each of N_2, N_1, N_0, N_{-1}, and N_{-2} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_2N_1N_0N_{-1}N_{-2}$-3', wherein each of N_2, N_1, N_0, N_{-1}, and N_{-2} is independently a nucleoside. In some embodiments, an oligonucleotide comprises 5'-$N_2N_1N_0N_{-1}N_{-2}$-3', wherein each of N_2, N_1, N_0, N_{-1}, and N_{-2} is independently a nucleoside, N_0 is opposite to a target adenosine, and each two of N_2, N_1, N_0, N_{-1}, and N_{-2} that are next to each other, as those skilled in the art will appreciate, independently bond to an internucleotidic linkage as described herein. In some embodiments, one or more or all of N_1, N_0, and N_{-1} independently have a natural RNA sugar. In some embodiments, one or more or all of N_1, N_0, and N_{-1} independently have a natural DNA sugar. In some embodiments, the sugar of each of N_1, N_0, and N_{-1} is independently a natural DNA sugar or a 2'-F modified sugar. In some embodiments, the sugar of each of N_1, N_0, and N_{-1} is independently a natural DNA sugar. In some embodiments, the sugar of N_1 is a 2'-modified sugar, and the sugar of each of N_0 and N_{-1} is independently a natural DNA sugar. In some embodiments, the sugar of N_1 is a 2'-F sugar, and the sugar of each of N_0 and N_{-1} is independently a natural DNA sugar. In some embodiments, the sugar of N_1 is a modified sugar. In some embodiments, the sugar of N_1 is a 2'-F modified sugar. In some embodiments, the sugar of N_1 is a natural DNA sugar. In some embodiments, the sugar of N_1 is a natural RNA sugar. In some embodiments, the sugar of N_0 is not a modified sugar. In some embodiments, the sugar of N_0 is not a 2'-modified sugar. In some embodiments, the sugar of N_0 is not a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, the sugar of N_0 is not a 2'-F modified sugar. In some

embodiments, the sugar of N_0 is not a 2'-OMe modified sugar. In some embodiments, the sugar of N_0 is a natural DNA or RNA sugar. In some embodiments, the sugar of N_0 is a natural DNA sugar. In some embodiments, the sugar of N_0 is a natural RNA sugar. In some embodiments, the sugar of N_{-1} is not a modified sugar. In some embodiments, the sugar of N_{-1} is not a 2'-modified sugar. In some embodiments, the sugar of N_{-1} is not a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, the sugar of N_{-1} is not a 2'-F modified sugar. In some embodiments, the sugar of N_{-1} is not a 2'-OMe modified sugar. In some embodiments, the sugar of N_{-1} is a natural DNA or RNA sugar. In some embodiments, the sugar of N_{-1} is a natural DNA sugar. In some embodiments, the sugar of N_{-1} is deoxyribose. In some embodiments, the sugar of N_{-1} is a natural RNA sugar. In some embodiments, each of N_1, N_0 and N_{-1} independently has a natural RNA sugar. In some embodiments, each of N_1, N_0 and N_{-1} independently has a natural DNA sugar. In some embodiments, N_1 has a 2'-F modified sugar, and each of N_0 and N_{-1} independently has a natural DNA or RNA sugar. In some embodiments, N_1 has a 2'-F modified sugar, and each of N_0 and N_{-1} independently has a natural DNA sugar(e.g., WV-22434). In some embodiments, two of N_1, N_0, and N_{-1} independently have a natural DNA or RNA sugar. In some embodiments, two of N_1, N_0, and N_{-1} independently have a natural DNA sugar. In some embodiments, each of N_1 and N_0 independently has a 2'-F modified sugar, and N_{-1} is a natural DNA sugar.

[00553] In some embodiments, such oligonucleotides provide high editing levels. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently *R*p. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently an *R*p phosphorothioate internucleotidic linkage. In some embodiments, each of the two internucleotidic linkages bonded to N_{-1} is independently an *R*p phosphorothioate internucleotidic linkage, and each other phosphorothioate internucleotidic linkage in an oligonucleotide, if any, is independently *S*p. In some embodiments, a 5' internucleotidic linkage bonded to N_1 is *R*p. In some embodiments, an internucleotidic linkage bonded to N_1 and N_0 (i.e., a 3' internucleotidic linkage bonded to N_1) is *R*p. In some embodiments, an internucleotidic linkage bonded to N_{-1} and N_0 is *R*p. In some embodiments, a 3' internucleotidic linkage bonded to N_{-1} is *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 or N_1 is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_0 or N_{-1} is independently *R*p. In some embodiments, each internucleotidic linkage bonded to N_1 is independently *R*p. In some embodiments, each *R*p internucleotidic linkage is independently an *R*p phosphorothioate internucleotidic linkage. In some embodiments, each other chirally controlled phosphorothioate internucleotidic linkage in an oligonucleotide is independently *S*p. In some embodiments, the internucleotidic linkage between N_0N_{-1} is *R*p. In some embodiments, the internucleotidic linkage between N_0N_{-1} is *R*p phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage between $N_{-1}N_{-2}$ is *R*p. In some embodiments, the internucleotidic linkage between $N_{-1}N_{-2}$ is *R*p phosphorothioate internucleotidic linkage. In some embodiments, all internucleotidic linkages bonded to N_1, N_0, and N_{-1} are independently *S*p. In some embodiments, all internucleotidic linkages bonded to N_1, N_0, and N_{-1} are independently *S*p phosphorothioate

internucleotidic linkages. In some embodiments, all internucleotidic linkages bonded to N_2, N_1, N_0, N_{-1}, and N_{-2} are independently *Sp*. In some embodiments, all internucleotidic linkages bonded to N_2, N_1, N_0, N_{-1}, and N_{-2} are independently *Sp* phosphorothioate internucleotidic linkages. In some embodiments, both internucleotidic linkage bonded to N_1 are independently *Sp* (e.g., *Sp* phosphorothioate internucleotidic linkages). In some embodiments, an internucleotidic linkage between N_1 and N_0 is *Sp* (e.g., a *Sp* phosphorothioate internucleotidic linkage). In some embodiments, an internucleotidic linkage between N_{-1} and N_0 is *Sp* (e.g., a *Sp* phosphorothioate internucleotidic linkage). In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is a neutral internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is n001. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is not chirally controlled. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is chirally controlled. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is *Rp*. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is *Sp*. In some embodiments, N_2 comprises a modified sugar. In some embodiments, N_{-2} comprises a modified sugar. In some embodiments, each of N_2 and N_{-2} independently comprises a modified sugar. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, a modified sugar is 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 2'-modified sugar is 2'-OMe modified sugar. In some embodiments, a 2'-modified sugar is 2'-MOE modified sugar. In some embodiments, a modified sugar is a bicyclic sugar, e.g., a LNA sugar, a cEt sugar, etc.

[00554] In some embodiments, to the 3'-side of a nucleoside opposite to a target adenosine (e.g., N_0) there are at least 2, 3, 4, 5, 6, 7, 8, 9 or more nucleosides (e.g., 2-30, 3-30, 4-30, 5-30, 2-20, 3-20, 4-20, 5-20, 2-15, 3-15, 4-15, 5-15, 2-10, 3-10, 4-10, 5-10, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc., "3'-side nucleosides"). In some embodiments, there are at least 2 3'-side nucleosides. In some embodiments, there are at least 3 3'-side nucleosides. In some embodiments, there are at least 4 3'-side nucleosides. In some embodiments, there are at least 5 3'-side nucleosides (e.g., an oligonucleotide comprising 5'-$N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}$-3', wherein each of N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, and N_{-5} is independently a nucleoside). In some embodiments, there are at least 6 3'-side nucleosides (e.g., an oligonucleotide comprising 5'-$N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}N_{-6}$-3', wherein each of N_0, N_{-1}, N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is independently a nucleoside). In some embodiments, there are at least 7 3'-side nucleosides. In some embodiments, there are at least 8 3'-side nucleosides. In some embodiments, there are at least 9 3'-side nucleosides. In some embodiments, there are at least 10 3'-side nucleosides. In some embodiments, there are 2 3'-side nucleosides. In some embodiments, there are 3 3'-side nucleosides. In some embodiments, there are 4 3'-side nucleosides. In some embodiments, there are 5 3'-side nucleosides. In some embodiments, there are 6 3'-side nucleosides. In some embodiments, there are 7 3'-side nucleosides. In some embodiments, there are 8 3'-side nucleosides. In some embodiments, there are 9 3'-side nucleosides. In some embodiments, there are 10 3'-side nucleosides. In some embodiments, to the 5'-side of a nucleoside opposite to a target adenosine (e.g., N_0) there are at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25,

26, 27, 28, 29 or 30 or more nucleosides (e.g., 15-50, 20-50, 21-50, 22-50, 23-50, 24-50, 25-50, 26-50, 27-50, 28-50, 29-50, 30-50, 15-40, 20-40, 21-40, 22-40, 23-40, 24-40, 25-40, 26-40, 27-40, 28-40, 29-40, 30-40, 15-30, 20-30, 21-30, 22-30, 23-30, 24-30, 25-30, 26-30, 27-30, 28-30, 29-30, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, there are at least 15 5'-side nucleosides. In some embodiments, there are at least 16 5'-side nucleosides. In some embodiments, there are at least 17 5'-side nucleosides. In some embodiments, there are at least 18 5'-side nucleosides. In some embodiments, there are at least 19 5'-side nucleosides. In some embodiments, there are at least 20 5'-side nucleosides. In some embodiments, there are at least 21 5'-side nucleosides. In some embodiments, there are at least 22 5'-side nucleosides. In some embodiments, there are at least 23 5'-side nucleosides. In some embodiments, there are at least 24 5'-side nucleosides. In some embodiments, there are at least 25 5'-side nucleosides. In some embodiments, there are at least 26 5'-side nucleosides. In some embodiments, there are at least 27 5'-side nucleosides. In some embodiments, there are at least 28 5'-side nucleosides. In some embodiments, there are at least 29 5'-side nucleosides. In some embodiments, there are at least 30 5'-side nucleosides. In some embodiments, there are 15 5'-side nucleosides. In some embodiments, there are 16 5'-side nucleosides. In some embodiments, there are 17 5'-side nucleosides. In some embodiments, there are 18 5'-side nucleosides. In some embodiments, there are 19 5'-side nucleosides. In some embodiments, there are 20 5'-side nucleosides. In some embodiments, there are 21 5'-side nucleosides. In some embodiments, there are 22 5'-side nucleosides. In some embodiments, there are 23 5'-side nucleosides. In some embodiments, there are 24 5'-side nucleosides. In some embodiments, there are 25 5'-side nucleosides. In some embodiments, there are 26 5'-side nucleosides. In some embodiments, there are 27 5'-side nucleosides. In some embodiments, there are 28 5'-side nucleosides. In some embodiments, there are 29 5'-side nucleosides. In some embodiments, there are 30 5'-side nucleosides. In some embodiments, there are at least 4 3'-side nucleosides and at least 22 5'-side nucleosides. In some embodiments, there are at least 4 3'-side nucleosides and at least 23 5'-side nucleosides. In some embodiments, there are at least 4 3'-side nucleosides and at least 24 5'-side nucleosides. In some embodiments, there are at least 4 3'-side nucleosides and at least 25 5'-side nucleosides. In some embodiments, there are at least 5 3'-side nucleosides and at least 22 5'-side nucleosides. In some embodiments, there are at least 5 3'-side nucleosides and at least 23 5'-side nucleosides. In some embodiments, there are at least 5 3'-side nucleosides and at least 24 5'-side nucleosides. In some embodiments, there are at least 5 3'-side nucleosides and at least 25 5'-side nucleosides. In some embodiments, there are at least 6 3'-side nucleosides and at least 21 5'-side nucleosides. In some embodiments, there are at least 6 3'-side nucleosides and at least 22 5'-side nucleosides. In some embodiments, there are at least 6 3'-side nucleosides and at least 23 5'-side nucleosides. In some embodiments, there are at least 6 3'-side nucleosides and at least 24 5'-side nucleosides. In some embodiments, there are at least 7 3'-side nucleosides and at least 20 5'-side nucleosides. In some embodiments, there are at least 7 3'-side nucleosides and at least 21 5'-side nucleosides. In some embodiments, there are at least 7 3'-side nucleosides and at least 22 5'-side nucleosides. In some embodiments, there are at least 7 3'-side nucleosides and at least 23 5'-side nucleosides. In some embodiments, there are at

least 8 3'-side nucleosides and at least 19 5'-side nucleosides. In some embodiments, there are at least 8 3'-side nucleosides and at least 20 5'-side nucleosides. In some embodiments, there are at least 8 3'-side nucleosides and at least 21 5'-side nucleosides. In some embodiments, there are at least 8 3'-side nucleosides and at least 22 5'-side nucleosides. In some embodiments, there are at least 9 3'-side nucleosides and at least 18 5'-side nucleosides. In some embodiments, there are at least 9 3'-side nucleosides and at least 19 5'-side nucleosides. In some embodiments, there are at least 9 3'-side nucleosides and at least 20 5'-side nucleosides. In some embodiments, there are at least 9 3'-side nucleosides and at least 21 5'-side nucleosides. In some embodiments, there are at least 10 3'-side nucleosides and at least 17 5'-side nucleosides. In some embodiments, there are at least 10 3'-side nucleosides and at least 18 5'-side nucleosides. In some embodiments, there are at least 10 3'-side nucleosides and at least 19 5'-side nucleosides. In some embodiments, there are at least 10 3'-side nucleosides and at least 20 5'-side nucleosides. In some embodiments, there are at least 11 3'-side nucleosides and at least 16 5'-side nucleosides. In some embodiments, there are at least 11 3'-side nucleosides and at least 17 5'-side nucleosides. In some embodiments, there are at least 11 3'-side nucleosides and at least 18 5'-side nucleosides. In some embodiments, there are at least 11 3'-side nucleosides and at least 19 5'-side nucleosides. In some embodiments, there are at least 12 3'-side nucleosides and at least 15 5'-side nucleosides. In some embodiments, there are at least 12 3'-side nucleosides and at least 16 5'-side nucleosides. In some embodiments, there are at least 12 3'-side nucleosides and at least 17 5'-side nucleosides. In some embodiments, there are at least 12 3'-side nucleosides and at least 18 5'-side nucleosides. In some embodiments, there are at least 13 3'-side nucleosides and at least 14 5'-side nucleosides. In some embodiments, there are at least 13 3'-side nucleosides and at least 15 5'-side nucleosides. In some embodiments, there are at least 13 3'-side nucleosides and at least 16 5'-side nucleosides. In some embodiments, there are at least 13 3'-side nucleosides and at least 17 5'-side nucleosides. In some embodiments, certain useful lengths of 5'-sides and/or 3'-sides and/or positioning of nucleosides opposite to target adenosines are described herein.

[00555] As described herein, wherein modifications may be utilized for N_1, including sugar modifications, nucleobase modifications, etc. In some embodiments, N_1 contains a natural DNA sugar. In some embodiments, N_1 contains a natural RNA sugar. In some embodiments, N_1 contains a modified sugar as described herein. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, a modified sugar is a 2'-F modified sugar. In some embodiments, a modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a modified sugar is a 2'-OMe modified sugar. In some embodiments, a modified sugar is a 2'-MOE modified sugar. In some embodiments, a sugar is a UNA sugar. In some embodiments, a sugar is a GNA sugar. In some embodiments, sugar of N_1 is sm01. In some embodiments, it is sm11. In some embodiments, it is sm12. In some embodiments, it is sm18. In some embodiments, a modified sugar, e.g., a 2'-F modified sugar, or a DNA sugar provides higher editing efficiency when administered to a system (e.g., a cell, a tissue, an organism, etc.) compared to a reference sugar

(e.g., a natural RNA sugar, a different modified sugar, etc.). In some embodiments, N_1 contains a natural nucleobase, e.g., U. In some embodiments, N_1 contains a modified nucleobase as described herein. In some embodiments, nucleobase of N_1 is A, T, C, G, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], or zdnp. In some embodiments, nucleobase of N_1 is T. In some embodiments, it is U. In some embodiments, it is b002A. In some embodiments, it is b003A. In some embodiments, it is b008U. In some embodiments, it is b010U. In some embodiments, it is b011U. In some embodiments, it is b012U. In some embodiments, it is b001C. In some embodiments, it is b004C. In some embodiments, it is b007C. In some embodiments, it is b008C. In some embodiments, N_1 is a natural nucleoside. In some embodiments, N_1 is a modified nucleoside. In some embodiments, N_1 is fU, dU, fA, dA, fT, dT, fC, dC, fG, dG, dI, fI, aC, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b010U, b011U, b012U, b013U, b014U, b015U, b001A, b001rA, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b003mC, b004C, b005C, b006C, b007C, b008C, b002I, b003I, b004I, b014I, Asm01, Gsm01, 5MSfC, Usm04, 5MRdT, Csm04, Csm11, Gsm11, Tsm11, b009Csm11, b009Csm12, Gsm12, Tsm12, Csm12, rCsm13, rCsm14, Csm15, Csm16, Csm17, L034, zdnp, and Tsm18. In some embodiments, N_1 is fU, dU, fA, dA, fT, dT, fC, dC, fG, dG, dI, or fI. In some embodiments, N_1 is fU, dU, fA, dA, fT, dT, fC, dC, fG, or dG. In some embodiments, N_1 is dT. In some embodiments, N_1 is b001A. In some embodiments, N_1 is b002A. In some embodiments, N_1 is b003A. In some embodiments, N_1 is b004A. In some embodiments, N_1 is b005A. In some embodiments, N_1 is b006A. In some embodiments, N_1 is fU. In some embodiments, N_1 is b008U. In some embodiments, N_1 is b001C. In some embodiments, N_1 is b004C. In some embodiments, N_1 is b007C. In some embodiments, N_1 is b008C. In some embodiments, N_1 is b001U. In some embodiments, N_1 is b008U. In some embodiments, N_1 is b010U. In some embodiments, N_1 is b011U. In some embodiments, N_1 is b012U. In some embodiments, N_1 is b013U. In some embodiments, N_1 is b014U. In some embodiments, N_1 is b015U. In some embodiments, N_1 is Csm11. In some embodiments, N_1 is Gsm11. In some embodiments, N_1 is Tsm11. In some embodiments, N_1 is b009Csm11. In some embodiments, N_1 is Csm12. In some embodiments, N_1 is Gsm12. In some embodiments, N_1 is Tsm12. In some embodiments, N_1 is b009Csm12. In some embodiments, N_1 is Gsm01. In some embodiments, N_1 is Tsm01. In some embodiments, N_1 is Csm17. In some embodiments, N_1 is Tsm18. In some embodiments, N_1 is b014I. In some embodiments, N_1 is abasic. In some embodiments, N_1 is L010. As described herein, at position N_1 in some embodiments, it is a match when an oligonucleotide forms a duplex with a nucleic acid (e.g., its target transcript for adenosine editing). In some embodiments, it is a mismatch. In some embodiments, it is a wobble. In some embodiments, N_1 is bonded to a natural phosphate linkage. In some embodiments, N_1 is bonded to a modified internucleotidic linkage as described herein, in various embodiments, with defined stereochemistry. In some embodiments, N_1 is bonded to a natural phosphate linkage and a modified internucleotidic linkage. In some embodiments, N_1 is

bonded to two natural phosphate linkages. In some embodiments, N_1 is bonded to two modified internucleotidic linkages, each of which may be independently and optionally stereocontrolled and may be *Rp* or *Sp*.

[00556] As described herein, wherein modifications may be utilized for N_{-1}, including sugar modifications, nucleobase modifications, etc. In some embodiments, N_{-1} contains a natural DNA sugar. In some embodiments, N_{-1} contains a natural RNA sugar. In some embodiments, N_{-1} contains a modified sugar as described herein. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, a modified sugar is a 2'-F modified sugar. In some embodiments, a modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a modified sugar is a 2'-OMe modified sugar. In some embodiments, a modified sugar is a 2'-MOE modified sugar. In some embodiments, a sugar is a UNA sugar. In some embodiments, a sugar is a GNA sugar. In some embodiments, sugar of N_{-1} is sm01. In some embodiments, it is sm11. In some embodiments, it is sm12. In some embodiments, it is sm18. In some embodiments, a modified sugar, e.g., a 2'-F modified sugar, or a DNA sugar provides higher editing efficiency when administered to a system (e.g., a cell, a tissue, an organism, etc.) compared to a reference sugar (e.g., a natural RNA sugar, a different modified sugar, etc.). In some embodiments, N_{-1} contains a natural nucleobase, e.g., U. In some embodiments, N_{-1} contains a modified nucleobase as described herein. In some embodiments, nucleobase of N_{-1} is A, T, C, G, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], or zdnp. In some embodiments, nucleobase of N_{-1} is T. In some embodiments, it is U. In some embodiments, it is b001A. In some embodiments, it is b002A. In some embodiments, it is b003A. In some embodiments, it is b004A. In some embodiments, it is b005A. In some embodiments, it is b006A. In some embodiments, it is b008U. In some embodiments, it is b011U. In some embodiments, it is b012U. In some embodiments, it is b013U. In some embodiments, it is b014U. In some embodiments, it is b015U. In some embodiments, it is b001C. In some embodiments, it is b004C. In some embodiments, it is b007C. In some embodiments, it is b008C. In some embodiments, it is b009C. In some embodiments, it is b002G. In some embodiments, it is b014I. In some embodiments, it is [3nT]. In some embodiments, it is [3ne5U]. In some embodiments, it is [3nfl5U]. In some embodiments, it is [3npry5U]. In some embodiments, it is [3ncn5U]. In some embodiments, it is [nathp608A]. In some embodiments, it is [ipr6o8A]. In some embodiments, it is [c7In]. In some embodiments, it is [c39z48In]. In some embodiments, it is [z2c3In]. In some embodiments, it is [z5C]. In some embodiments, with the high flexibility and efficiency of technologies described herein, various nucleobases and sugars can be utilized at N_{-1} to provide editing. For example, as confirmed, various nucleobases, e.g., G, b006C, b007C, b004A, b007A, b002I, b003I, b004I, etc., and/or various sugars, e.g., natural DNA sugars, sm11, sm12, etc., can be utilized at N_{-1}, which is opposite to C, to provide editing, in some embodiments, with higher editing levels compared to certain other nucleobases and/or

sugars; and various nucleobases, e.g., C, b008U, b005U, b009U, b012U, b005C, b008C, b001A, b004A, b007A, b002I, b004I, b001G, abasic, etc., and/or various sugars, e.g., natural DNA sugars, sm11, sm12, sm15, etc., can be utilized at N_{-1}, which is opposite to G, to provide editing, in some embodiments, with higher editing levels compared to certain other nucleobases and/or sugars; and various nucleobases, e.g., A, b004U, b009U, b010U, b011U, b012U, b006C, b008C, b009C, b001A, b003A, b004A, b006A, b007A, b003I, b004I, b001G, abasic, etc., and/or various sugars, e.g., natural DNA sugars, sm11, sm12, sm15, etc., can be utilized at N_{-1}, which is opposite to U/T, to provide editing, in some embodiments, with higher editing levels compared to certain other nucleobases and/or sugars; and various nucleobases, e.g., U, T, b003U, b004U, b005U, b008U, b009U, b010U, b011U, b012U, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b001A, b003A, b004A, b006A, b007A, b002I, b003I, b004I, b001G, b002G, abasic, etc., and various sugars, e.g., natural DNA sugar, sm11, sm12, sm15, sm17, etc., can be utilized at N_{-1} which is opposite to A, to provide editing, in some embodiments, with higher editing levels compared to certain other nucleobases and/or sugars. In some embodiments, nucleobase G can be utilized to opposite C at N_{-1} to provide effective editing, e.g., when the nucleobase of N_0 is b008U. In some embodiments, N_0 is b008U and N_{-1} is G. In some embodiments, when a neighboring nucleoside (e.g., 5'-side) of a target adenosine is A, certain nucleobases, sugars, etc. at N_{-1} position (opposite to a 5' neighboring adenosine) provide higher editing efficiency and/or selectivity compared to others. In some embodiments, certain nucleobases, e.g., b008U, at N_0 provide target adenosine editing with higher selectivity over a neighboring A (e.g., a 5'-side A) compared to other nucleobases, e.g., C. In some embodiments, N_0 is b008U to provide editing efficiency and selectivity. In some embodiments, N_{-1} is a natural nucleoside. In some embodiments, N_{-1} is a modified nucleoside. In some embodiments, N_{-1} is fU, dU, fA, dA, fT, dT, fC, dC, fG, dG, dI, fI, aC, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b010U, b011U, b012U, b013U, b014U, b015U, b001A, b001rA, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b003mC, b004C, b005C, b006C, b007C, b008C, b002I, b003I, b004I, b014I, Asm01, Gsm01, 5MSfC, Usm04, 5MRdT, Csm04, Csm11, Gsm11, Tsm11, b009Csm11, b009Csm12, Gsm12, Tsm12, Csm12, rCsm13, rCsm14, Csm15, Csm16, Csm17, L034, zdnp, and Tsm18. In some embodiments, N_{-1} is fU, dU, fA, dA, fT, dT, fC, dC, fG, dG, dI, or fI. In some embodiments, N_{-1} is fU, dU, fA, dA, fT, dT, fC, dC, fG, or dG. In some embodiments, N_{-1} is dI. In some embodiments, N_{-1} is rI. In some embodiments, N_{-1} is dT. In some embodiments, N_{-1} is b001A. In some embodiments, N_{-1} is b002A. In some embodiments, N_{-1} is b003A. In some embodiments, N_{-1} is b004A. In some embodiments, N_{-1} is b005A. In some embodiments, N_{-1} is b006A. In some embodiments, N_{-1} is b007A. In some embodiments, N_{-1} is fU. In some embodiments, N_{-1} is b001C. In some embodiments, N_{-1} is b002C. In some embodiments, N_{-1} is b003C. In some embodiments, N_{-1} is b004C. In some embodiments, N_{-1} is b005C. In some embodiments, N_{-1} is b006C. In some embodiments, N_{-1} is b007C. In some embodiments, N_{-1} is b008C. In some embodiments, N_{-1} is b009Csm12. In some embodiments, N_{-1} is b001G. In some embodiments, N_{-1} is b002G. In some embodiments, N_{-1} is b001U. In some embodiments, N_{-1} is b003U. In some embodiments, N_{-1} is b004U. In some embodiments, N_{-1} is b005U. In some embodiments, N_{-1} is b006U. In some embodiments, N_{-1} is b007U.

In some embodiments, N_{-1} is b008U. In some embodiments, N_{-1} is b009U. In some embodiments, N_{-1} is b010U. In some embodiments, N_{-1} is b011U. In some embodiments, N_{-1} is b012U. In some embodiments, N_{-1} is b013U. In some embodiments, N_{-1} is b014U. In some embodiments, N_{-1} is b015U. In some embodiments, N_{-1} is b002I. In some embodiments, N_{-1} is b003I. In some embodiments, N_{-1} is b004I. In some embodiments, N_{-1} is Gsm01. In some embodiments, N_{-1} is Tsm01. In some embodiments, N_{-1} is Csm11. In some embodiments, N_{-1} is b009Csm11. In some embodiments, N_{-1} is Gsm11. In some embodiments, N_{-1} is Tsm11. In some embodiments, N_{-1} is Csm12. In some embodiments, N_{-1} is b009Csm12. In some embodiments, N_{-1} is Gsm12. In some embodiments, N_{-1} is Tsm12. In some embodiments, N_{-1} is Csm17. In some embodiments, N_{-1} is Tsm18. In some embodiments, N_{-1} is abasic. In some embodiments, N_{-1} is L010. In some embodiments, N_{-1} is b002G. In some embodiments, N_{-1} is b014I. As described herein, at position N_{-1} in some embodiments, it is a match when an oligonucleotide forms a duplex with a nucleic acid (e.g., its target transcript for adenosine editing). In some embodiments, it is a mismatch. In some embodiments, it is a wobble. In some embodiments, N_{-1} is bonded to a natural phosphate linkage. In some embodiments, N_{-1} is bonded to a modified internucleotidic linkage as described herein, in various embodiments, with defined stereochemistry. In some embodiments, N_{-1} is bonded to a natural phosphate linkage and a modified internucleotidic linkage. In some embodiments, N_{-1} is bonded to two natural phosphate linkages. In some embodiments, N_{-1} is bonded to two modified internucleotidic linkages, each of which may be independently and optionally stereocontrolled and may be *R*p or *S*p.

[00557] In some embodiments, N_2 contains a natural sugar. In some embodiments, sugar of N_2 is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00558] In some embodiments, an internucleotidic linkage between N_1 and N_2 is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001.

[00559] In some embodiments, N_3 contains a natural sugar. In some embodiments, sugar of N_3 is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00560] In some embodiments, an internucleotidic linkage between N_2 and N_3 is a natural phosphate

linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001. In some embodiments, N_4 contains a natural sugar. In some embodiments, sugar of N_4 is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00561] In some embodiments, an internucleotidic linkage between N_3 and N_4 is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001.

[00562] In some embodiments, N_5 contains a natural sugar. In some embodiments, sugar of N_5 is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00563] In some embodiments, an internucleotidic linkage between N_4 and N_5 is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001.

[00564] In some embodiments, N_6 contains a natural sugar. In some embodiments, sugar of N_6 is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00565] In some embodiments, an internucleotidic linkage between N_5 and N_6 is a natural phosphate

linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *Sp*. In some embodiments, it is *Rp*. In some embodiments, it is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, it is *Sp* n001. In some embodiments, it is *Rp* n001.

[00566] As described herein, an oligonucleotide, or a portion thereof, e.g., a first domain, a second domain, etc., may comprise or consist of one or more, e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc. blocks, each of which independently comprises one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-24, 1-23, 1-22, 1-21, 1-20, 1-10, 1-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, etc.) sugars, wherein each sugar in a block share the same structure. In some embodiments, an oligonucleotide, or a portion thereof, e.g., a first domain, a second domain, etc., may comprise or consist of one or more, e.g., 1-20, 1-15, 1-14, 1-13, 1-12, 1-11, 1-10, 2-20, 3-15, 4-15, 5-15, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc. blocks, each of which independently comprises one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-24, 1-23, 1-22, 1-21, 1-20, 1-10, 1-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, etc.) sugars, wherein each sugar in a block is the same modified sugar. In some embodiments, each block independently contains 1-10, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, sugars. In some embodiments, each block independently contains 1-5 sugars. In some embodiments, each block independently contains 1, 2, or 3 sugars. In some embodiments, one or more blocks, e.g., 1-15, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, independently contain two or three or more sugars. In some embodiments, one or more blocks, e.g., 1-15, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, independently contain two or three sugars. In some embodiments, about or at least about 30%, 40% or 50% blocks in an oligonucleotide or a portion thereof independently contains two or more (e.g., two or three) sugars. In some embodiments, about 50% blocks in an oligonucleotide of a first domain independently contains two or more (e.g., two or three) sugars. In some embodiments, a block is a 2'-F block wherein each sugar in the block is a 2'-F modified block. In some embodiments, a block is a 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic wherein each sugar in the block is the same 2'-OR modified sugar. In some embodiments, a block is a 2'-OMe block. In some embodiments, a block is a 2'-MOE block. In some embodiments, a block is a bicyclic sugar block wherein each sugar in the block is the same bicyclic sugar (e.g., a LNA sugar, cEt, etc.). In some embodiments, two or more blocks are 2'-F blocks. In some embodiments, every other block is a 2'-F block. In some embodiments, each 2'-F block independently contains no more than 2, 3, 4, 5, 6, 7, 8, 9, or 10 sugars. In some embodiments, a 2'-F block contains no more than 5 sugars. In some embodiments, a 2'-F block contains no more than 4 sugars. In some embodiments, a 2'-F block contains no more than 3 sugars. In some embodiments, between every two 2'-F blocks in an oligonucleotide or a portion thereof there is at least one 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic or one bicyclic sugar

block. In some embodiments, between every two 2'-F blocks in a portion there is at least one 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic or one bicyclic sugar block. In some embodiments, between every two 2'-F blocks in an oligonucleotide there is at least one 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, between every two 2'-F blocks in a first domain there is at least one 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, between every two 2'-F blocks in a first domain there is at least one 2'-OMe block. In some embodiments, between two 2'-F blocks in a first domain there is a 2'-OMe block. In some embodiments, between two 2'-F blocks in a first domain there is a 2'-MOE block. In some embodiments, between two 2'-F blocks in a first domain there is a 2'-MOE block and 2'-OMe block. In some embodiments, between two 2'-F blocks in a first domain there is a 2'-MOE block and 2'-OMe block and no 2'-F block. In some embodiments, each 2'-F block is independently bonded to a 2'-OR block wherein R is C_{1-6} aliphatic or a bicyclic sugar block. In some embodiments, each 2'-F block is independently bonded to a 2'-OR block wherein R is C_{1-6} aliphatic. In some embodiments, each block a 2'-F block bonds to is independently a 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar block. In some embodiments, each block a 2'-F block bonds to is independently a 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each block in a first domain that a 2'-F block in a first domain bonds to is independently a 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar block. In some embodiments, each block in a first domain that a 2'-F block in a first domain bonds to is independently a 2'-OR block wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each block in a first domain that a 2'-OR block wherein R is C_{1-6} aliphatic or a bicyclic sugar block bonds is independently a 2'-F block of a different 2'-OR block wherein R is C_{1-6} aliphatic or a bicyclic sugar block. In some embodiments, each block in a first domain that a 2'-OR block wherein R is C_{1-6} aliphatic bonds is independently a 2'-F block of a different 2'-OR block wherein R is C_{1-6} aliphatic. In some embodiments, a 2'-OR block is a 2'-OMe block. In some embodiments, a 2'-OR block is a 2'-MOE block. In some embodiments, at least one block is a 2'-OMe block. In some embodiments, about or about at least 2, 3, 4, or 5 blocks are independently 2'-OMe block. In some embodiments, at least one block is a 2'-MOE block. In some embodiments, about or about at least 2, 3, 4, or 5 blocks are independently 2'-MOE block. In some embodiments, in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OMe block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-MOE block. In some embodiments, in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OMe block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-MOE block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-F block. In some embodiments, in a first domain there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OMe block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-MOE block. In some embodiments, in a first domain there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OMe block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-F block. In some embodiments, in a first domain there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-F block

and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-MOE block. In some embodiments, in a first domain there are one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-OMe block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more) 2'-MOE block and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-F block. In some embodiments, in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., percentage of 2'-F modified sugars is about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80%, and percentage of 2'-OR modified sugars each of which is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic is about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80%. In some embodiments, in a first domain percentage of 2'-F modified sugars is about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80%, and percentage of 2'-OR modified sugars each of which is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic is about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80%. In some embodiments, the difference between the percentage of 2'-F modified sugars and the percentage of 2'-OR modified sugars each of which is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic is less than about 50%, 40%, 30%, 20%, or 10% (calculated by subtracting the smaller of the two percentages from the larger of the two percentages). In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or 2'-MOE modified sugar.

[00567] For example, in some embodiments, sugar of each of N_2, N_5, and N_6 is independently a 2'-F modified sugar, and sugar of each of N_3 and N_4 is independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, sugar of each of N_2, N_5, and N_6 is independently a 2'-F modified sugar, and sugar of each of N_3 and N_4 is independently a 2'-OR modified sugar. In some embodiments, sugar of each of N_2, N_5, and N_6 is independently a 2'-F modified sugar, and sugar of each of N_3 and N_4 is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, sugar of each of N_2, N_5, and N_6 is independently a 2'-F modified sugar, and sugar of each of N_3 and N_4 is independently a 2'-OMe modified sugar. In some embodiments, at least one sugar is a 2'-MOE modified sugar. In some embodiments, sugar of N_3 is a 2'-MOE modified sugar. In some embodiments, sugar of N_3 is a 2'-OMe modified sugar. In some embodiments, sugar of N_4 is a 2'-MOE modified sugar. In some embodiments, sugars of both N_3 and N_4 are 2'-MOE modified sugar. In some embodiments, N_2 forms a 2'-F block. In some embodiments, N_3 and N_4 forms a 2'-OMe block. In some embodiments, N_3 and N_4 forms a 2'-MOE block. In some embodiments, N_5, N_6 and/or N_7 form a 2'-F block. As demonstrated herein, oligonucleotides comprising modified sugars, e.g., 2'-F modified sugars, 2'-OMe modified sugars, 2'-MOE modified sugars, etc., at various positions can provide, among other things, high levels of adenosine editing. For example, 2'-MOE modified sugars can be incorporated at various positions to provide oligonucleotides capable of adenosine editing; in some embodiments, sugar of N_1 is a 2'-MOE modified sugar; in some embodiments, sugar of N_2 is a 2'-MOE modified sugar; in some embodiments, sugar of N_3 is a 2'-MOE modified sugar; in some embodiments, sugar of N_4 is a 2'-MOE modified sugar; in some embodiments, sugar of N_5 is a 2'-MOE modified sugar; in some

embodiments, sugar of N_6 is a 2'-MOE modified sugar; in some embodiments, sugar of N_7 is a 2'-MOE modified sugar; in some embodiments, sugar of N_8 is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-1} is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-2} is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-3} is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-4} is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-5} is a 2'-MOE modified sugar; in some embodiments, sugar of N_{-6} is a 2'-MOE modified sugar.

[00568] As described herein, various internucleotidic linkages may be utilized in oligonucleotides or portions thereof, e.g., first domains, second domains, etc. For example, various linkages may be utilized in first domains. In some embodiments, a first domain comprises one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more natural phosphate linkages. In some embodiments, a first domain comprises one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, modified internucleotidic linkages. In some embodiments, a first domain comprises one or more natural phosphate linkages and one or more modified internucleotidic linkages. In some embodiments, one or more modified internucleotidic linkages are phosphorothioate internucleotidic linkages. In some embodiments, each phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc. is *Sp*. In some embodiments, each phosphorothioate internucleotidic linkage in an oligonucleotide is *Sp*. In some embodiments, one or more modified internucleotidic linkages are independently non-negatively charged internucleotidic linkage. In some embodiments, one or more modified internucleotidic linkages are independently non-negatively charged internucleotidic linkage. In some embodiments, one or more modified internucleotidic linkages are independently phosphoryl guanidine internucleotidic linkages. In some embodiments, each phosphoryl guanidine internucleotidic linkage is independently n001. In some embodiments, a first domain contains about 1-5, e.g., 1, 2, 3, 4, or 5 non-negatively charged internucleotidic linkages. In some embodiments, each of such non-negatively charged internucleotidic linkages are independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, each of them is independently n001. In some embodiments, one or more of them are independently chirally controlled. In some embodiments, each of them is chirally controlled. In some embodiments, each of them is *Rp* n001. In some embodiments, one or more sugars that are 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic are bonded to natural phosphate linkages. In some embodiments, one or more 2'-OMe sugars are bonded to natural phosphate linkages. In some embodiments, one or more 2'-MOE sugars are bonded to natural phosphate linkages. In some embodiments, one or more 2'-F modified sugars are bonded to natural phosphate linkages. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-OMe modified sugars in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., are independently

bonded to a natural phosphate linkage. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-MOE modified sugars in an oligonucleotide or a portion thereof, e.g., a first domain, a second domain, etc., are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic in a first domain, a second domain are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-OMe modified sugars in a first domain are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 20%, 30%, 40%, 50%, 60%, 70%, 80% or 90% 2'-MOE modified sugars in a first domain are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 1-10, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, 2'-OR modified sugars wherein R is optionally substituted C_{1-6} aliphatic in a first domain, a second domain are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 1-10, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, 2'-OMe modified sugars in a first domain are independently bonded to a natural phosphate linkage. In some embodiments, about or at least about 1-10, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, 2'-MOE modified sugars in a first domain are independently bonded to a natural phosphate linkage. In some embodiments, one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more, natural phosphate linkage bonded to a 2'-F modified sugar are independently bonded to a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, each natural phosphate linkage bonded to a 2'-F modified sugar is independently bonded to a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more, natural phosphate linkages bonded to a 2'-F modified sugar is independently bonded to a 2'-MOE modified sugar. In some embodiments, each natural phosphate linkage bonded to a 2'-F modified sugar is independently bonded to a 2'-MOE modified sugar.

[00569] Among other things, the present disclosure demonstrates that oligonucleotides comprising various blocks and patterns as described herein, e.g., 2'-F blocks, 2'-OMe blocks, 2'-MOE blocks, etc., and/or various internucleotidic linkages and patterns thereof as described herein, can provide improved pharmacodynamics, pharmacokinetics, and/or adenosine editing levels, etc., compared to comparable reference oligonucleotides, e.g., those previously reported in WO 2016/097212, WO 2017/220751, WO 2018/041973, WO 2018/134301A1, WO 2019/158475, WO 2019/219581, WO 2020/157008, WO 2020/165077, WO 2020/201406 or WO 2020/252376. In some embodiments, a reference oligonucleotide is an oligonucleotide reported in WO 2021/071858. In some embodiments, a reference oligonucleotide is an oligonucleotide reported in WO 2022/099159.

[00570] In some embodiments, N_{-2} contains a natural sugar. In some embodiments, sugar of N_{-2} is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00571] In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *Sp*. In some embodiments, it is *Rp*. In some embodiments, it is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, it is *Sp* n001. In some embodiments, it is *Rp* n001. In some embodiments, N_{-1} is dI, and a linkage between N_{-1} and N_{-2} is a *Sp* phosphoryl guanidine internucleotidic linkage. In some embodiments, N_{-1} is dI, and a linkage between N_{-1} and N_{-2} is *Sp* n001.

[00572] In some embodiments, N_{-3} contains a natural sugar. In some embodiments, sugar of N_{-3} is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00573] In some embodiments, an internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *Sp*. In some embodiments, it is *Rp*. In some embodiments, it is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, it is *Sp* n001. In some embodiments, it is *Rp* n001.

[00574] In some embodiments, N_{-4} contains a natural sugar. In some embodiments, sugar of N_{-4} is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00575] In some embodiments, an internucleotidic linkage between N_{-3} and N_{-4} is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *Sp*. In some embodiments, it is *Rp*. In some embodiments, it is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, it is *Sp* n001. In some embodiments, it is *Rp* n001.

[00576] In some embodiments, N_{-5} contains a natural sugar. In some embodiments, sugar of N_{-5} is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein

R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00577] In some embodiments, an internucleotidic linkage between N_{-4} and N_{-5} is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001.

[00578] In some embodiments, N_{-6} contains a natural sugar. In some embodiments, sugar of N_{-6} is a natural DNA sugar. In some embodiments, it is a natural RNA sugar. In some embodiments, it is a modified sugar. In some embodiments, it is a 2'-F modified sugar. In some embodiments, it is a 2'-OR modified sugar, wherein R is C_{1-6} aliphatic as described herein. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, it is a 2'-OMe modified. In some embodiments, it is a 2'-MOE modified sugar.

[00579] In some embodiments, an internucleotidic linkage between N_{-5} and N_{-6} is a natural phosphate linkage. In some embodiments, it is a modified internucleotidic linkage. In some embodiments, it is a phosphorothioate internucleotidic linkage. In some embodiments, it is a non-negatively charged internucleotidic linkage. In some embodiments, it is a neutral internucleotidic linkage. In some embodiments, it is phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is *S*p. In some embodiments, it is *R*p. In some embodiments, it is a *S*p phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p n001. In some embodiments, it is *R*p n001.

[00580] In some embodiments, linkage phosphorus of a natural phosphate linkage in an oligonucleotide is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside. In some embodiments, linkage phosphorus of a natural phosphate linkage in an oligonucleotide is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside, wherein the nucleoside comprises a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, linkage phosphorous of each natural phosphate linkage in an oligonucleotide is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside. In some embodiments, linkage phosphorous of each natural phosphate linkage in an oligonucleotide is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside, wherein the nucleoside comprises a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

[00581] In some embodiments, at least one sugar of N_{-1}, N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a natural DNA sugar. In some embodiments, at least one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-F modified sugar. In some embodiments, at least one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, at least one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-OMe modified sugar. In some embodiments, at least one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-MOE modified sugar. In some embodiments, at least one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a bicyclic sugar, e.g., a LNA

sugar, a cEt sugar, etc. In some embodiments, one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-F modified sugar, and each of the other sugars are independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic (e.g., a 2'-OMe modified sugar, a 2'-MOE modified sugar, etc.) or a bicyclic sugar as described herein. In some embodiments, one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-F modified sugar, and each of the other sugars are independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-F modified sugar, and each of the other sugars are independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, one sugar of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is a 2'-F modified sugar, and each of the other sugars are independently a 2'-OMe modified sugar. In some embodiments, sugar of N_{-3} a 2'-F modified sugar. In some embodiments, sugar of N_{-1} is a DNA sugar, sugar of N_{-3} is a 2'-F modified sugar, and sugar of each of N_{-2}, N_{-4}, N_{-5}, and N_{-6} is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar (e.g., a LNA sugar, an ENA sugar, etc.) as described herein. In some embodiments, sugar of N_{-1} is a DNA sugar, sugar of N_{-3} is a 2'-F modified sugar, and sugar of each of N_{-2}, N_{-4}, N_{-5}, and N_{-6} is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, sugar of N_{-1} is a DNA sugar, sugar of N_{-3} is a 2'-F modified sugar, and sugar of each of N_{-2}, N_{-4}, N_{-5}, and N_{-6} is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, sugar of N_{-1} is a DNA sugar, sugar of N_{-3} is a 2'-F modified sugar, and sugar of each of N_{-2}, N_{-4}, N_{-5}, and N_{-6} is independently a 2'-OMe modified sugar. In some embodiments, N_{-2} forms a 2'-OMe block. In some embodiments, N_{-3} forms a 2'-F block. In some embodiments, N_{-4}, N_{-5}, and N_{-6} forms a 2'-OMe block.

[00582] In some embodiments, at least one of N_{-2}, N_{-3}, N_{-4}, N_{-5}, and N_{-6} is bonded to a natural phosphate linkage. In some embodiments, a linkage between N_{-2} and N_{-3} is a natural phosphate linkage. In some embodiments, N_{-2} is bonded to a non-negatively charged internucleotidic linkage. In some embodiments, at least one of N_{-3}, N_{-4}, N_{-5}, and N_{-6} is bonded to a non-negatively charged internucleotidic linkage. In some embodiments, a linkage between N_{-5} and N_{-6} is a non-negatively charged internucleotidic linkage. In some embodiments, at least one of N_{-3}, N_{-4}, N_{-5}, and N_{-6} is bonded to a phosphorothioate internucleotidic linkage. In some embodiments, each of N_{-3}, N_{-4} and N_{-5} is independently bonded to a phosphorothioate internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001. In some embodiments, it is *Rp*. In some embodiments, it is *Sp*. In some embodiments, a phosphorothioate internucleotidic linkage is *Rp*. In some embodiments, a phosphorothioate internucleotidic linkage is *Sp*. In some embodiments, each phosphorothioate internucleotidic linkage is *Sp*. In some embodiments, a linkage between N_{-2} and v-3 is a natural phosphate linkage, a linkage between N_{-3} and N_{-4} is a *Sp* phosphorothioate internucleotidic linkage, a linkage between N_{-4} and N_{-5} is a *Sp* phosphorothioate internucleotidic linkage, and a linkage between N_{-5} and N_{-6} is a *Rp* non-negatively charged internucleotidic linkage (e.g., a *Rp* phosphoryl guanidine internucleotidic linkage such as *Rp* n001). In some embodiments, a natural phosphate linkage is bonded to at least one modified sugar. In some embodiments, a natural phosphate linkage is bonded to at least

one 2'-OR modified sugar wherein R is C_{1-6} aliphatic or a bicyclic sugar. In some embodiments, a natural phosphate linkage is bonded to a 2'-OMe modified sugar. In some embodiments, a natural phosphate linkage is bonded to a 2'-MOE modified sugar. In some embodiments, both sugars bonded to a natural phosphate linkage is independently a modified sugar as described herein.

[00583] In some embodiments, an oligonucleotide comprises a first domain as described herein (e.g., a first domain in which multiple or a majority of or all of sugars are 2'-F modified sugars) and a second domain as described herein (e.g., a second domain in which multiple or a majority of or all of sugars are non-2'-F modified sugars (e.g., 2'-OMe modified sugars)). In some embodiments, a first domain is at the 5' side of a second domain. In some embodiments, a first domain is at the 3' side of a second domain. In some embodiments, when a first domain is at the 3' side of a second domain, there is at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more (e.g., 1-20, 2-20, 3-20, 4-20, 5-20, 6-20, 7-20, 7-11, etc.) 5'-side nucleosides of a nucleoside opposite to a target adenosine. In some embodiments, there are at least 3. In some embodiments, there are at least 4. In some embodiments, there are at least 5. In some embodiments, there are at least 6. In some embodiments, there are at least 7. In some embodiments, there are at least 8. In some embodiments, there are at least 9. In some embodiments, there are at least 10. In some embodiments, there are 3. In some embodiments, there are 4. In some embodiments, there are 5. In some embodiments, there are 6. In some embodiments, there are 7. In some embodiments, there are 8. In some embodiments, there are 9. In some embodiments, there are 10. In some embodiments, there are 11. In some embodiments, there are 7-11. In some embodiments, there are 9-11. In some embodiments, there are 10 or 11. In some embodiments, additionally or alternatively, there are at least 15, 16, 17, 18, 19, 20 or more (e.g., 15-30, 16-30, 17-30, 18-30, 18-25, 18-22, etc.) 5'-side nucleosides of a nucleoside opposite to a target adenosine. In some embodiments, there are at least 15. In some embodiments, there are at least 16. In some embodiments, there are at least 17. In some embodiments, there are at least 18. In some embodiments, as described above, there are at least about 5 (e.g., 5-50, 5-40, 5-30, 5-20, 5-10, 5-9, 5, 6, 7, 8, 9, or 10, etc.) 3'-side nucleosides and at least about 15 (e.g., 15-50, 15-40, 15-30, 15-20, 20-30, 20-25, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.) 5'-side nucleosides. In some embodiments, independently about 1-10 (e.g., 2-10, 3-10, 3-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) bicyclic or 2'-OR modified sugars are independently on the 5'-, or 3'-, or both sides of an editing region (e.g., $N_1N_0N_{-1}$), wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, independently about 1-10 (e.g., 2-10, 3-10, 3-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-OR modified sugars are independently on the 5'-, or 3'-, or both sides of an editing region, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, independently about 1-10 (e.g., 2-10, 3-10, 3-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) 2'-OMe modified sugars are independently on the 5'-, or 3'-, or both sides of an editing region. In some embodiments, they are on the 5' side. In some embodiments, they are on the 3' sides. In some embodiments, they are on both sides. In some embodiments, it is beneficial that surrounding an editing region, e.g., $N_1N_0N_{-1}$, there are bicyclic or 2'-OR modified sugars, e.g., independently about 1-10 (e.g., 2-10, 3-10, 3-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10), on both sides, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, it is beneficial that

surrounding an editing region, e.g., $N_1N_0N_{-1}$, there are 2'-OR modified sugars, e.g., independently about 1-10 (e.g., 2-10, 3-10, 3-5, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10), on both sides, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, on each side there are at least 2. In some embodiments, each 2'-OR modified sugar is a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is a 2'-MOE modified sugar.

[00584] One of the many advantages of provided technologies is that much shorter oligonucleotides compared to traditional technologies of others can provide comparable or higher levels of adenosine editing. Those skilled in the art reading the present disclosure will appreciate that longer oligonucleotides (e.g., extending 5' side, 3' side or both sides of a target adenosine) incorporating one or more structural elements (e.g., sugar modifications, nucleobase modifications, internucleotidic linkage modifications, stereochemistry, and/or patterns thereof) of oligonucleotides of the present disclosure may also be useful, e.g., for various uses described herein including adenine editing and prevention and/or treatment of conditions, disorders or diseases which can benefit editing of target adenosines.

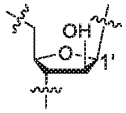
[00585] In some embodiments, ADAR1 p150 may tolerate variations of lengths of 5'-sides and/or 3'-sides and/or positioning of nucleosides opposite to target adenosines more than ADAR1 p110. In some embodiments, the present disclosure provides particularly useful lengths of 5'-sides and/or 3'-sides and/or positioning of nucleosides opposite to target adenosines for editing (e.g., by ADAR1 p110 and/or ADAR1 p150). In some embodiments, certain useful lengths of 5'-sides and/or 3'-sides and/or positioning of nucleosides (e.g., of those oligonucleotides that provide editing, such as WV-12027, WV-42028, WV-42029, WV-42030, WV-42032, and WV-420333; in some embodiments, of WV-42027; in some embodiments, of WV-42028; in some embodiments, of WV-42029; in some embodiments, of WV-42030; in some embodiments, of WV-42031) are useful for editing in cells expressing ADAR1, e.g., ADAR1 p110 and/or p150. For oligonucleotide structures, see, e.g., WO 2022/099159.

[00586] In some embodiments, each phosphorothioate bonded to a nucleoside opposite to a target adenosine is independently a phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_0 and N_{-1} is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, the internucleotidic linkage between N_{-1} and N_{-2} is a *R*p phosphorothioate internucleotidic linkage.

[00587] In some embodiments, the present disclosure provides oligonucleotides comprising editing regions that can provide high editing efficiency. In some embodiments, a provided editing region is or comprises 5'-$N_1N_0N_{-1}$–3' as described herein.

[00588] In some embodiments, the present disclosure provides oligonucleotides comprising 5'-$N_1N_0N_{-1}$–3' as described herein.

[00589] In some embodiments, N_0 is as described herein. In some embodiments, N_0 comprises a sugar and a nucleobase as described herein. In some embodiments, N_0 has a natural DNA sugar. In some embodiments, N_0 has a natural RNA sugar. In some embodiments, N_0 has a modified sugar, e.g., a 2'-F modified sugar. In

some embodiments, sugar of a nucleobase opposite to a target adenosine, or N_0, is arabinofuranose. In some embodiments, sugar of a nucleobase opposite to a target adenosine, or N_0, is , wherein C1' bonds to a nucleobase as described herein. In some embodiments, N_0 has a natural nucleobase. In some embodiments, nucleobase of N_0 is C. In some embodiments, nucleobase of N_0 is b001A. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is cytidine. In some embodiments, N_0 is 2'-F C (wherein 2'-OH of cytidine is replaced with -F). In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, nucleobase of N_0 is not T or U. In some embodiments, nucleobase of N_0 is not T. In some embodiments, nucleobase of N_0 is not U. In some embodiments, N_0 is not a match to A.

[00590] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*.

[00591] In some embodiments, nucleobase of N_1 is T, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is thymidine, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*.

[00592] In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*.

[00593] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is guanine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyguanosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as

deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*. In some embodiments, there are 6 or at least 6 nucleosides to the 3' side of N_0 (e.g., when there are 6, N_{-1} to N_{-6}).

[00594] In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is guanine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyguanosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*. In some embodiments, there are 6 or at least 6 nucleosides to the 3' side of N_0 (e.g., when there are 6, N_{-1} to N_{-6}).

[00595] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_0 is as described herein such as cytosine, b001A, b008U, etc. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*A -3' for editing a target adenosine *A*.

[00596] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F U, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is thymine. In some embodiments, N_1 is 2'-F C, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-A*A*A -3' for editing a target adenosine *A*.

[00597] In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F A, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F G, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F A, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F A, and N_{-1} is dC. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-A*A*U -3' for editing a target adenosine *A*.

[00598] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F U, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F C, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F C, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-A*A*G -3' for editing a target adenosine *A*.

[00599] In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F G, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F G, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-A*A*C -3' for editing a target adenosine *A*.

[00600] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F U, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-U*A*A -3' for editing a target adenosine *A*.

[00601] In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F U, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-U*A*U -3' for editing a target adenosine *A*.

[00602] In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F U, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F C, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F C, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA,

b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-U*A*G -3' for editing a target adenosine *A*.

[00603] In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F G, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F U, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F G, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-U*A*C -3' for editing a target adenosine *A*.

[00604] In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F C, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-G*A*A -3' for editing a target adenosine *A*.

[00605] In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F A, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, N_0 is as described herein such as

deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-G*A*U -3' for editing a target adenosine *A*.

[00606] In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F C, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F C, and N_{-1} is dC. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-G*A*G -3' for editing a target adenosine *A*.

[00607] In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is T. In some embodiments, N_1 is 2'-F G, and N_{-1} is dT. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is C. In some embodiments, N_1 is 2'-F G, and N_{-1} is dC. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-G*A*C -3' for editing a target adenosine *A*.

[00608] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F A, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15.

In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*U -3' for editing a target adenosine *A*.

[00609] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F U, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F C, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*G -3' for editing a target adenosine *A*.

[00610] In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F A, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F G, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is G. In some embodiments, N_1 is 2'-F G, and N_{-1} is dG. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, N_0 is as described herein such as deoxycytidine, b001A, Csm15, b001rA, b008U, etc. In some embodiments, N_0 is deoxycytidine. In some embodiments, N_0 is b001A. In some embodiments, N_0 is Csm15. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-C*A*C -3' for editing a target adenosine *A*.

[00611] In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F U, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F C, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is G, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F G, and N_{-1} is dA. In some embodiments, nucleobase of N_1 is C, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F C, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is U, and nucleobase of N_{-1} is hypoxanthine. In some embodiments, N_1 is 2'-F U, and N_{-1} is deoxyinosine. In some embodiments, nucleobase of N_1 is A, and nucleobase of N_{-1} is A. In some embodiments, N_1 is 2'-F A, and N_{-1} is dA. In some embodiments, N_0 is b001rA. In some embodiments, N_0 is b008U. In some embodiments, such 5'-$N_1N_0N_{-1}$–3'are particularly useful for targeting RNA comprising 5'-U*A*G -3' for editing a target adenosine *A*.

[00612] In some embodiments, nucleobase U may be replaced with T without lowering editing levels. In some embodiments, nucleobase U may be replaced with T to increase editing levels. In some embodiments, 2'-F U may be replaced with thymidine. In some embodiments, N_1 is thymidine. In some embodiments, N_1 is thymidine, N_0 is as described herein, e.g., b001A, b008U, etc. In some embodiments, N_1 is thymidine, N_0 is as described herein, e.g., b001A, b008U, etc., and N_{-1} is I.

[00613] In some embodiments, when being aligned to a target sequence and/or hybridized to a target nucleic acid, N_0 is a wobble or mismatch to A. In some embodiments, N_1 is not a match to its opposite nucleobase. In some embodiments, N_{-1} is not a match to its opposite nucleobase. In some embodiments, two of N_{-1}, N_0 and N_1 are independently not a match to its opposite nucleobase. In some embodiments, N_0 and N_1 are independently not a match to its opposite nucleobase. In some embodiments, N_0 and N_{-1} are independently not a match to its opposite nucleobase. In some embodiments, when it is not a match, it is a wobble. In some embodiments, when it is not a match, it is a mismatch. In some embodiments, nucleobase of N_1 is C and its opposite nucleobase is A. In some embodiments, more nucleosides to the 3' side of N_0 (e.g., 6 or more) may tolerate more mismatches/wobbles of 5'-$N_1N_0N_{-1}$-3'.

[00614] In some embodiments, each internucleotidic linkage bonded to N_0 is independently *Sp* phosphorothioate internucleotidic linkages. In some embodiments, each internucleotidic linkage bonded to N_1 is independently *Sp* phosphorothioate internucleotidic linkages. In some embodiments, an internucleotidic linkage bonded to N_{-1} is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage bonded to N_{-1} is a neutral internucleotidic linkage. In some embodiments, an internucleotidic linkage bonded to N_{-1} is a phosphoryl guanidine internucleotidic linkage. In some embodiments, an internucleotidic linkage bonded to N_{-1} is n001. In some embodiments, a phosphoryl guanidine internucleotidic linkage, e.g., n001, bonded to N_{-1} (e.g., to its position 3') is chirally controlled and is *Rp*. In some embodiments, a phosphoryl guanidine internucleotidic linkage, e.g., n001, bonded to N_{-1} (e.g., to its position 3') is chirally controlled and is *Sp* (e.g., in some embodiments, when N_{-1} is dI).

Base Sequences

[00615] As appreciated by those skilled in the art, structural features of the present disclosure, such as nucleobase modification, sugar modifications, internucleotidic linkage modifications, linkage phosphorus stereochemistry, etc., and combinations thereof may be utilized with various suitable base sequences to provide oligonucleotides and compositions with desired properties and/or activities. For example, oligonucleotides for adenosine modification (e.g., conversion to I in the presence of ADAR proteins) typically have sequences that are sufficiently complementary to sequences of target nucleic acids that comprise target adenosines. Nucleosides opposite to target adenosines can be present at various positions of oligonucleotides. In some embodiments, one or more opposite nucleosides are in first domains. In some embodiments, one or more opposite nucleosides are in second domains. In some embodiments, one or more opposite nucleosides are in first subdomains. In some embodiments, one or more opposite nucleosides are in second subdomains. In some embodiments, one or more opposite nucleosides are in third subdomains. Oligonucleotide of the present

disclosure may target one or more target adenosines. In some embodiments, one or more opposite nucleosides are each independently in a portion which has the structure features of a second subdomain, and each independently have one or more or all structural features of opposite nucleosides as described herein. In many embodiments, oligonucleotides may selectively target one and only one target adenosine for modification, e.g., by ADAR to convert into I. In some embodiments, an opposite nucleoside is closer to the 3'-end than to the 5'-end of an oligonucleotide.

[00616] In some embodiments, an oligonucleotide has a base sequence described herein (e.g., in a Table) or a portion thereof (e.g., a span of 10-50, 10-40, 10-30, 10-20, or 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or at least 10, at least 15, at least 20, at least 25 contiguous nucleobases) with 0-5 (e.g., 0, 1, 2, 3, 4 or 5) mismatches, wherein each T can be independently substituted with U and vice versa. In some embodiments, an oligonucleotide comprises a base sequence described herein, or a portion thereof, wherein a portion is a span of at least 10 contiguous nucleobases, or a span of at least 15 contiguous nucleobases with 0-5 mismatches. In some embodiments, provided oligonucleotides have a base sequence described herein, or a portion thereof, wherein a portion is a span of at least 10 contiguous nucleobases, or a span of at least 10 contiguous nucleobases with 1-5 mismatches, wherein each T can be independently substituted with U and vice versa.

[00617] In some embodiments, base sequences of oligonucleotides comprise or consist of 10-60 (e.g., about or at least 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60; in some embodiments, at least 15; in some embodiments, at least 16; in some embodiments, at least 17; in some embodiments, at least 18; in some embodiments, at least 19; in some embodiments, at least 20; in some embodiments, at least 21; in some embodiments, at least 22; in some embodiments, at least 23; in some embodiments, at least 24; in some embodiments, at least 25; in some embodiments, at least 26; in some embodiments, at least 27; in some embodiments, at least 28; in some embodiments, at least 29; in some embodiments, at least 30; in some embodiments, at least 31; in some embodiments, at least 32; in some embodiments, at least 33; in some embodiments, at least 34; in some embodiments, at least 35) bases, optionally contiguous, of a base sequence that is identical or complementary to a base sequence of a nucleic acid (e.g., a PNPLA3 nucleic acid), e.g., a gene or a transcript (e.g., mRNA) thereof. In some embodiments, the base sequence of an oligonucleotide is or comprises a sequence that is complementary to a target sequence in a gene (e.g., PNPLA3) or a transcript thereof. In some embodiments, the sequence is 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 55, 60 or more nucleobases in length.

[00618] In some embodiments, a target sequence is or comprises a characteristic sequence of a PNPLA3 nucleic acid sequence (e.g., of an gene or a transcript thereof) in that it defines the PNPLA3 nucleic acid sequence over others in a relevant organism; for example, a characteristic sequence is not in or has at least various mismatches from other genomic nucleic acid sequences (e.g., genes) or transcripts thereof in a relevant organism. In some embodiments, a characteristic sequence of a PNPLA3 transcript defines that transcript over

other transcripts in a relevant organism; for example, in some embodiments, a characteristic sequence is not in transcripts that are transcribed from a different nucleic acid sequence (e.g., a different gene). In some embodiments, PNPLA3 transcript variants from a nucleic acid sequence (e.g., mRNA variants of a gene) may share a common characteristic sequence that defines them from, e.g., transcripts of other genes. In some embodiments, a characteristic sequence comprises a target adenosine. In some embodiments, an oligonucleotide selectively forms a duplex with a nucleic acid comprising a target adenosine, wherein the target adenosine is within the duplex region and can be modified by a protein such as ADAR1 or ADAR2.

[00619] Base sequences of provided oligonucleotides, as appreciated by those skilled in the art, typically have sufficient lengths and complementarity to their target nucleic acids (e.g., PNPLA3 nucleic acids), e.g., RNA transcripts (e.g., pre-mRNA, mature mRNA, etc.) for, e.g., site-directed editing of target adenosines. In some embodiments, an oligonucleotide is complementary to a portion of a target PNPLA3 RNA sequence comprising a target adenosine (as appreciated by those skilled in the art, in many instances target nucleic acids are longer than oligonucleotides of the present disclosure, and complementarity may be properly assessed based on the shorter of the two, oligonucleotides). In some embodiments, the base sequence of an oligonucleotide has 90% or more identity with the base sequence of an oligonucleotide disclosed in a Table, wherein each T can be independently substituted with U and vice versa. In some embodiments, the base sequence of an oligonucleotide has 95% or more identity with the base sequence of an oligonucleotide disclosed in a Table, wherein each T can be independently substituted with U and vice versa. In some embodiments, the base sequence of an oligonucleotide comprises a continuous span of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40 or more bases of an oligonucleotide disclosed in a Table, wherein each T can be independently substituted with U and vice versa, except that one or more bases within the span are abasic (e.g., a nucleobase is absent from a nucleotide).

[00620] In some embodiments, the present disclosure pertains to an oligonucleotide having a base sequence which comprises the base sequence of any oligonucleotide disclosed herein, wherein each T may be independently replaced with U and vice versa.

[00621] In some embodiments, the present disclosure pertains to an oligonucleotide having a base sequence which is the base sequence of any oligonucleotide disclosed herein, wherein each T may be independently replaced with U and vice versa.

[00622] In some embodiments, the present disclosure pertains to an oligonucleotide having a base sequence which comprises at least 15 contiguous bases of the base sequence of any oligonucleotide disclosed herein, wherein each T may be independently replaced with U and vice versa.

[00623] In some embodiments, the present disclosure pertains to an oligonucleotide having a base sequence which is at least 90% identical to the base sequence of any oligonucleotide disclosed herein, wherein each T may be independently replaced with U and vice versa.

[00624] In some embodiments, the present disclosure pertains to an oligonucleotide having a base sequence which is at least 95% identical to the base sequence of any oligonucleotide disclosed herein, wherein each T

may be independently replaced with U and vice versa.

[00625] In some embodiments, a base sequence of an oligonucleotide is, comprises, or comprises 10-40, e.g., 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40 contiguous bases of the base sequence of any oligonucleotide described herein, wherein each T may be independently replaced with U and vice versa.

[00626] In some embodiments, an oligonucleotide is an oligonucleotide presented in a Table herein.

[00627] In some embodiments, the base sequence of an oligonucleotide is complementary to that of a target nucleic acid, e.g., a portion comprising a target adenosine.

[00628] In some embodiments, an oligonucleotide has a base sequence which comprises at least 15 contiguous bases (e.g., 15, 16, 17, 18, 19, or 20) of an oligonucleotide in a Table, wherein each T can be independently substituted with U and vice versa.

[00629] In some embodiments, an oligonucleotide comprises a base sequence or portion thereof (*e.g.*, a portion comprising 10-40, e.g., 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40 nucleobases) described in a Table, wherein each T may be independently replaced with U and vice versa, and/or a sugar, nucleobase, and/or internucleotidic linkage modification and/or stereochemistry, and/or a pattern thereof described in a Table, and/or an additional chemical moiety (in addition to an oligonucleotide chain, e.g., a target moiety, a lipid moiety, a carbohydrate moiety, etc.) described in any of the Tables.

[00630] In some embodiments, the terms "complementary," "fully complementary" and "substantially complementary" may be used with respect to the base matching between an oligonucleotide and a target sequence, as will be understood by those skilled in the art from the context of their uses. It is noted that substitution of T for U, or vice versa, generally does not alter the amount of complementarity. As used herein, an oligonucleotide that is "substantially complementary" to a target sequence is largely or mostly complementary but not necessarily 100% complementary. In some embodiments, a sequence (e.g., an oligonucleotide) which is substantially complementary has one or more, e.g., 1, 2, 3, 4 or 5 mismatches when maximally aligned to its target sequence. In some embodiments, an oligonucleotide has a base sequence which is substantially complementary to a target sequence of a target nucleic acid. In some embodiments, an oligonucleotide has a base sequence which is substantially complementary to the complement of the sequence of an oligonucleotide disclosed herein. As appreciated by those skilled in the art, in some embodiments, sequences of oligonucleotides need not be 100% complementary to their targets for oligonucleotides to perform their functions (e.g., converting A to I in a nucleic acid. In some embodiments, a mismatch is well tolerated at the 5' and/or 3' end or the middle of an oligonucleotide. In some embodiments, one or more mismatches are preferred for adenosine modification as demonstrated herein. In some embodiments, oligonucleotides comprise portions for complementarity to target nucleic acids, and optionally portions that are not primarily for complementarity to target nucleic acids; for example, in some embodiments, oligonucleotides may comprise portions for protein binding. In some embodiments, base sequences of provided oligonucleotides

are fully complementary to their target sequences (A-T/U and C-G base pairing). In some embodiments, base sequences of provided oligonucleotides are fully complementary to their target sequences (A-T/U and C-G base pairing) except at a nucleoside opposite to a target nucleoside (e.g., adenosine).

[00631] In some embodiments, the present disclosure provides an oligonucleotide comprising a sequence found in an oligonucleotide described in a Table, wherein one or more U is independently and optionally replaced with T or vice versa. In some embodiments, an oligonucleotide can comprise at least one T and/or at least one U. In some embodiments, the present disclosure provides an oligonucleotide comprising a sequence found in an oligonucleotide described in a Table herein, wherein the said sequence has over 50% identity with the sequence of the oligonucleotide described in a Table. In some embodiments, the present disclosure provides an oligonucleotide whose base sequence is the sequence of an oligonucleotide disclosed in a Table, wherein each T may be independently replaced with U and vice versa. In some embodiments, the present disclosure provides an oligonucleotide comprising a sequence found in an oligonucleotide in a Table, wherein the oligonucleotides have a pattern of backbone linkages, pattern of backbone chiral centers, and/or pattern of backbone phosphorus modifications of the same oligonucleotide or another oligonucleotide in a Table herein.

[00632] In some embodiments, the disclosure provides an oligonucleotide having a base sequence which is, comprises, or comprises a portion of the base sequence of an oligonucleotide disclosed herein, e.g., in a Table, wherein each T may be independently replaced with U and vice versa, wherein the oligonucleotide optionally further comprises a chemical modification, stereochemistry, format, an additional chemical moiety described herein (e.g., a targeting moiety, lipid moiety, carbohydrate moiety, etc.), and/or another structural feature.

[00633] In some embodiments, a "portion" (e.g., of a base sequence or a pattern of modifications or other structural element) is at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 monomeric units long.

[00634] Those skilled in the art reading the present disclosure will appreciate that technologies herein may be utilized to target various target nucleic acids comprising target adenosine for editing. In some embodiments, oligonucleotides of the present disclosure have suitable base sequences so that they have sufficient complementarity to selectively form duplexes with a portion of a transcript that comprise the target adenosine for editing.

[00635] As described herein, nucleosides opposite to target nucleosides (e.g., A) can be positioned at various locations. In some embodiments, an opposite nucleoside is at position 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 3 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 4 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 5 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 6 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 7 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 8 or more from the 5'-end of an oligonucleotide. In some embodiments, it is at position 9 or more from the 5'-end of an oligonucleotide. In some embodiments,

it is at position 10 or more from the 5'-end of an oligonucleotide. In some embodiments, an opposite nucleoside is at position 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 3 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 4 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 5 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 6 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 7 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 8 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 9 or more from the 3'-end of an oligonucleotide. In some embodiments, it is at position 10 or more from the 3'-end of an oligonucleotide. In some embodiments, nucleobases at position 1 from the 5'-end and/or the 3'-end are complementary to corresponding nucleobases in target sequences when aligned for maximum complementarity. In some embodiments, certain positions, e.g., position 6, 7, or 8, may provide higher editing efficiency.

[00636] As examples, certain oligonucleotides comprising certain example base sequences, nucleobase modifications and patterns thereof, sugar modifications and patterns thereof, internucleotidic linkages and patterns thereof, linkage phosphorus stereochemistry and patterns thereof, linkers, and/or additional chemical moieties, etc., are presented in Table 1 and Table 1A, below. Among other things, these oligonucleotides may be utilized to introduce an A to I variation (e.g., to generate an alternative amino acid codon). In some embodiments, listed in Tables are stereorandom oligonucleotide compositions. In some embodiments, the present disclosure provides chirally controlled oligonucleotide compositions.

[00637] In some embodiments, a base sequence is or comprises a particular sequence. In some embodiments, a base sequence is complementary to a base sequence that is or comprises a base sequence that is complementary to a particular sequence. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 1, 2, 3, 4, or 5 positions. In some embodiments, a base sequence is or comprise a sequence that differs from about 15-30 (e.g., 15-25, 15-20, 20-30, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) consecutive nucleobases of a particular sequence at no more than 1, 2, 3, 4, or 5 positions. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 1 position. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 2 positions. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 3 positions. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 4 positions. In some embodiments, a base sequence is or comprise a sequence that differs from a particular sequence at no more than 5 positions. In some embodiments, a particular sequence is or comprises a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 5-30, 10-30, 15-30, 20-30, or 25-30 (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments,

a particular sequence is or comprises 10 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 11 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 12 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 13 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 14 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 15 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 16 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 17 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 18 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 19 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 20 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 21 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 22 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 23 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 24 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 25 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 26 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 27 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 28 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 29 consecutive bases in a base sequence or the base sequence of an oligonucleotide selected from Table 1 or Table 1A. In some embodiments, a particular sequence is or comprises 30 consecutive bases or the base sequence of an oligonucleotide in a base sequence selected from Table 1 or Table 1A. In some embodiments, an oligonucleotide can hybridize to a portion (e.g., about 20-100, 30-60, 20-50, or about

20, 30, 40, 50, 60, or 70 bases, or of a length of an oligonucleotide) in a target mRNA, which portion comprises a base sequence that is complementary to the base sequence of an oligonucleotide described herein, e.g., in a Table. In some embodiments, an oligonucleotide can hybridize to a portion (e.g., about 20-100, 30-60, 20-50, or about 20, 30, 40, 50, 60, or 70 bases, or of a length of an oligonucleotide) in a target mRNA which portion can hybridize to an oligonucleotide described herein, e.g., in a Table.

[00638] Certain oligonucleotides and/or compositions are described in Table 1 and Table 1A below.

Table 1. Example oligonucleotides and/or compositions.

ID	HELM Description
ADR-0107818	RNA1{m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107819	RNA1{m(G)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107820	RNA1{m(A)[n001R].m(U)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].m(C)[Ssp].m(A)[n001R].m(G)}$$$$V2.0
ADR-0107821	RNA1{m(G)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107822	RNA1{m(A)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107823	RNA1{m(A)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107831	RNA1{m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107832	RNA1{m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}$$$$V2.0
ADR-	RNA1{m(A)[n001R].m(U)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](

0107833	C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].m(C)[Ssp].m(A)[n001R].m(G)}$$$$V2.0
ADR-0107834	RNA1{m(G)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107835	RNA1{m(A)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0107836	RNA1{m(A)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)[Ssp].[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$$V2.0
ADR-0108477	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108478	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108479	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108481	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)[Ssp].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108482	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)p.[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108483	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)

	[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108484	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[Ssp].[fl2r](G)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108485	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)p.m(A)[Ssp].[fl2r](C)[n001R].m(U)p.[fl2r](G)[Ssp].[fl2r](U)[n001R].[fl2r](A)p.m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108486	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])p.[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.m(C)[n001R].m(U)p.[fl2r](G)[Ssp].[fl2r](U)[n001R].[fl2r](A)p.[moe](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].m(G)p.[moe]([m5C])p.[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108487	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])p.[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[moe](T)p.[fl2r](C)[n001R].m(U)p.[fl2r](G)[Ssp].[fl2r](U)[n001R].[fl2r](A)p.[moe](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[n001R].[moe](G)p.[moe]([m5C])p.[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108488	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108489	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108490	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108491	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)[Ssp].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108492	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)p.[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)

	[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108493	RNA1{p.m(A)[n001R].m(U)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(C)[Ssp].m(A)[n001R].m(G)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108494	RNA1{p.m(U)[n001R].m(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].m(G)[n001R].m(G)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108495	RNA1{p.m(A)[n001R].m(A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].m(G)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108497	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108498	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108499	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108500	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108501	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108502	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ss

	p].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108503	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108504	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(G)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108505	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108506	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108507	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108508	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108509	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108510	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r

0108511	](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108512	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108513	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108514	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108517	RNA1{p.m(G)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108518	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[Ssp].m(A)[n001R].m(G)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

Table 1A. Example oligonucleotides and/or compositions.

ID	HELM Description
ADR-0110420	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110686	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.m(U)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110687	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].m(A)p.m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].

	m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110688	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110689	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].m(G)p.[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110690	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110691	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110692	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110693	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110694	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110425	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0110695	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110696	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110697	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110698	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110699	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110700	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110701	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110702	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].m(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110703	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].m(G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110704	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110705	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110706	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110707	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110708	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110709	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110710	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.m(U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110711	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110712	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,

	RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110713	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110714	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110715	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110716	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110717	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110718	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110719	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.d(T)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110720	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110721	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].d(G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)

	p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110722	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d(C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110723	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].d(C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110724	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110725	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].d(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110726	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].d(T)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110727	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110728	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.d(T)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110729	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].d(G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110730	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].d(G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[S

	sp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110731	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110732	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].d(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110733	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].d(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110734	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].d(G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110735	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].d(G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110736	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110737	RNA1{p.d(G)[n001R].d(G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110738	RNA1{p.d(G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110739	RNA1{p.[moe](G)[n001R].d(G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001

	R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110740	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.d(T)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110741	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].d(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110742	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].d(A)[Ssp].d(G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110743	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d(C)[Ssp].d(C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110744	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].d(C)[Ssp].d(A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110745	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110746	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].d(C)[n001R].d(T)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110747	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].d(T)[n001R].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0110748	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].d(G)p.d(T)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110749	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.d(T)[Ssp].d(G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110750	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].d(G)[Ssp].d(G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110751	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].d(G)[Ssp].d(A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110752	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].d(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110753	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].d(A)[Ssp].d(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110754	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].d(A)[Ssp].d(G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110755	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].d(G)[Ssp].d(G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110756	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110757	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110758	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110759	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[n001R].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110760	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[n001R].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110761	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[n001R].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110762	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110763	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110424	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110426	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$C

	HEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110764	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110765	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110766	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110767	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110768	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110769	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[n001R].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110770	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d([Hyp])[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110771	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[lr](G)[n001R].[lr]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110772	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(

	A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110773	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110774	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110775	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109982	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110517	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110518	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110519	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110520	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110521	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[

	Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110522	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110523	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110524	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110525	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110526	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110527	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110528	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109982	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110402	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n

	001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110403	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110404	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110405	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110406	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110407	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110408	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110409	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110410	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0110411	r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110412	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110413	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110414	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110415	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110416	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110417	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110418	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110419	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110420	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110421	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110422	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110423	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110424	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110425	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110426	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110427	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110428	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12o

	vl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110429	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110430	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110431	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110432	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110433	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110434	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110435	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110436	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12ovl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110437	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A

	)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110438	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110439	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110440	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110441	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110442	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110443	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110444	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110445	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110446	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].

	[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110447	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110448	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110449	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110450	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110451	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110452	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110453	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110454	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110455	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n00

	1R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110456	RNA1{p.m(G)[n001R].m(G)[Ssp].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110457	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110458	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110459	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110460	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110461	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110462	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](U)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110463	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](

0110464	G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110465	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110466	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110467	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110468	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110469	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](G)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110470	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(U)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110471	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[lr](G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110472	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].[lr]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110473	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[lr](G)[n001R].[lr]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110474	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110475	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[moe](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110476	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[moe](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110477	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110478	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].m(A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110479	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[lr](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110480	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[lr](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110481	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RN

	A1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110482	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110483	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110484	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110485	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110486	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110487	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])[n001R].[moe](T)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110488	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])[n001R].[moe](T)[n001R].[moe](G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110489	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110490	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)

	p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110491	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110492	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110493	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110494	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110495	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])[n001R].[moe](T)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110496	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])[n001R].[moe](T)[n001R].[moe](G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.m(A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108477	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0108479	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109971	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](

	A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109972	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109973	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109974	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109975	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109976	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].[fl2r](G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109977	RNA1{p.[moe](G)[n001R].[moe](G)[Ssp].[moe](A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109978	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109979	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[moe](G)[n001R].[moe]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109980	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n

	001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[moe](G)[n001R].[moe]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109981	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109982	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109983	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109984	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109985	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].m(G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109986	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].m(C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109987	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109988	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](

0109989	G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109990	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109991	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109992	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109993	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109994	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109995	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109996	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109997	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0109998	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109999	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110000	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110001	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].m(A)p.m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110002	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110003	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].m(G)p.m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110004	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110005	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110006	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,R

	NA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110007	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110008	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110009	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110010	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110011	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110012	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110013	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110014	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110015	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl

	2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110016	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110017	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110018	RNA1{p.m(G)[n001R].m(G)[n001R].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110019	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110020	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110021	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110022	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110023	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[n001R].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110024	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2

	r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110025	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[n001R].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110026	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[n001R].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110027	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[n001R].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110028	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110029	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110030	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110031	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110032	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110033	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n00

	1R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110034	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110035	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110036	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110037	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[n001R].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110038	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110039	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[moe](A)p.m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110040	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[moe](A)p.[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110041	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[moe](G)p.m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](

0110042	G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110043	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[moe]([m5C])p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110044	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[moe]([m5C])p.[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110045	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[moe](A)p.[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110046	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[moe]([m5C])p.[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110047	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[moe](T)p.m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110048	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].[moe](G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110049	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[moe](T)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110050	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[moe](A)p.[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110051	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[moe](G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110052	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[moe](A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110053	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[moe](A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110054	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[moe](A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110055	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[moe](G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110056	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110057	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[moe]([m5C])p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110651	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[Ir](G)[n001R].[Ir]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110652	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1

	-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110653	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110654	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110655	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110656	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110657	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110658	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110659	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110660	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.m(G)p.[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110661	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[n001R].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].

	m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110662	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.m(A)p.[fl2r](G)[n001R].m(G)p.m(C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110663	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110664	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110665	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110482	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110666	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[lr](G)[n001R].[lr]([m5C])}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110667	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110668	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110669	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].

	m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110670	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110671	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110672	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110673	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110674	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110675	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.m(G)p.[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110676	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[n001R].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110677	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.m(A)p.[fl2r](G)[n001R].m(G)p.m(C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110678	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001

	R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110679	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110680	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110420	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110681	RNA1{p.[moe](G)[n001R].[moe](A)p.[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110682	RNA1{p.[moe](A)[n001R].[moe](T)p.[moe](A)p.m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110683	RNA1{p.[moe](T)[n001R].[moe](A)p.[moe](A)p.[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110684	RNA1{p.[moe](A)[n001R].[moe](A)p.[moe](G)p.[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110685	RNA1{p.[moe](G)[n001R].[moe](A)p.[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](

0109982	G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110420	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110424	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110867	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110868	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110869	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110870	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110871	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110872	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110873	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110874	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110875	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110876	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110877	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110878	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110879	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110880	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110881	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110882	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110883	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110884	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110885	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110886	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110887	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110888	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110889	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110890	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001

	R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110891	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110892	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110893	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110894	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110895	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110896	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)[n001R].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110897	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110898	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110899	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r

	](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110900	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110901	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110902	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110903	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110904	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110905	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110906	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110907	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110908	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p

	.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110909	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110910	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110911	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110912	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110913	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110914	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110915	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110916	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[S

0110917	sp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110918	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110919	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110920	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110921	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110922	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110923	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110924	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110925	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0110926	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)p.[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110927	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)p.[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110928	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)p.[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110929	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)p.[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110930	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)p.[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110931	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110932	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110933	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110934	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110639	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110640	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n003R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110641	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n008R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110642	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n078R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110643	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n025R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110644	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n026R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110645	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n003R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110646	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n008R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110647	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n078R

	].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$ CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110648	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$ CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110649	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](G)[n001R].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n026R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$ CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0109971	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110369	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110370	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].[lr](G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110371	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$ CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110372	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[moe](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110373	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[moe](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110374	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

	A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110375	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].m(A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110376	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ir](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110377	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ir](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110378	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110379	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d([Hyp])[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110380	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Sgna](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110381	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Rgna](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110382	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Sgna](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110383	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n00

	1R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Rgna](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110384	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Sgna](G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110385	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Rgna](G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110386	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Sgna](G)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110390	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[m1d](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110391	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[m1d](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110392	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[m1d](G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110393	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[m1d](G)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110394	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d([purine])[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Sgna](G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

0110395	G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d([purine])p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110396	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ld](A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110397	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ld](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110398	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ld](G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110399	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[Ld](G)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0110401	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[una](A)p.m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111098	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111099	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111100	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0111101	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111102	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111103	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)[n001R].m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111104	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.m(C)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111105	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111106	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)[n001R].m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111107	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111108	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111109	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111110	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111111	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111112	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111113	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)[n001R].m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111114	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m(C)p.m(C)p.m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111115	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111116	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111117	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.m(U)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.m(C)p.d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111118	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].

	m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111119	RNA1{p.m(G)[n001R].m(G)[Ssp].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111120	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].m(A)p.[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[n001R].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111121	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111122	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111123	RNA1{p.[moe](G)[n001R].[moe](A)p.[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111124	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111125	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111126	RNA1{p.[moe](G)[n001R].[moe](A)p.[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].m(A)[n001R].[fl2r](G)[Ssp].[fl2r](G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111127	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)

	[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111128	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111129	RNA1{p.[moe](G)[n001R].[moe](A)p.[moe](T)p.[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.[fl2r](C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111130	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111131	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111132	RNA1{p.[moe](G)[n001R].[moe](A)[Ssp].[moe](T)[n001R].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(A)p.[fl2r](A)[n001R].[fl2r](G)[Ssp].m(G)p.[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111133	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].m(G)[Ssp].[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111134	RNA1{p.m(G)[n001R].m(A)[Ssp].m(U)[n001R].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111135	RNA1{p.[moe](G)[n001R].[moe](A)[Ssp].[moe](T)[n001R].[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].m(C)p.m(A)p.m(C)[n001R].[fl2r](U)[Ssp].m(G)[n001R].[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].m(A)p.m(A)p.m(A)[n001R].[fl2r](G)[Ssp].m(G)[n001R].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[Ssp].m(C)[n001R].m(A)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111136	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R]

	.m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111137	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111138	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111139	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111140	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].d(T)[n001R].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111141	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111142	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111143	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111144	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0111145	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111146	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111147	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111148	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111149	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111150	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].d(T)[n001R].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111151	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111152	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111153	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0111154	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111155	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111156	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111157	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111158	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111159	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111160	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].d(T)[Ssp].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111161	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111162	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111163	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111164	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111165	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111166	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111167	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111168	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111169	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111170	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111171	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].d(T)[Ssp].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G

	)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111172	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111173	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111174	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111175	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[Ssp].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n025R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111179	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111180	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111181	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111182	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111183	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].d(T)[n001R].d(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ss

	p].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111184	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111185	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111309	RNA1{p.[m1d](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111310	RNA1{p.[moe](G)[n001R].[m1d](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111311	RNA1{p.[moe](G)[n001R].[moe](G)p.[m1d](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111312	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[m1d](T)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111313	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[m1d](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111314	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].[m1d](A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111315	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[m1d](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001

	R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111316	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[m1d](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111317	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[m1d](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111318	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[m1d](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111319	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[m1d](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111320	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[m1d](C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111321	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[m1d](T)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111322	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].[m1d](G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111323	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[m1d](T)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0111324	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[m1d](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111325	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].[m1d](G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111326	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[m1d](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111327	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].[m1d](A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111328	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[m1d](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111329	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[m1d](G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111330	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[m1d](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111331	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m(G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[m1d](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111774	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0111775	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](A)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111776	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111777	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(U)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111778	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](C)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111779	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe]([m5C])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111780	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111781	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111782	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111783	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111784	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111785	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(C)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111786	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111787	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111788	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111789	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111790	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111791	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111792	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m

	(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111793	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111794	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111795	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(T)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111796	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(C)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111797	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.d([Hyp])[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111798	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(G)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111799	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111800	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].d([Hyp])[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111801	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].d([Hyp])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp]

	.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111802	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111803	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111804	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111805	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(U)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111806	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].d([Hyp])[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111807	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].d([Hyp])p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111808	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.d([Hyp])[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111809	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].d([Hyp])p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111810	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m

	(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111811	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111812	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111813	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].d([Hyp])[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111814	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].d([Hyp])[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111815	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111816	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111817	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d([Hyp])[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111818	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0111819	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111820	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111821	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(U)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111822	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](C)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111823	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe]([m5C])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111824	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111825	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111826	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111827	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0111828	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(A)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111829	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(C)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111830	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111831	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111832	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111833	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111834	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111835	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111836	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111837	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111838	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111839	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(T)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111840	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(C)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111841	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.d([Hyp])[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111842	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111843	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111844	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].d([Hyp])[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111845	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].d([Hyp])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(

	G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111846	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111847	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111848	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111849	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(U)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111850	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].d([Hyp])[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111851	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].d([Hyp])p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111852	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.d([Hyp])[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111853	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].d([Hyp])p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111854	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp]

	.[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111855	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111856	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111857	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].d([Hyp])[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111858	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].d([Hyp])[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111859	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111860	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(G)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111861	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d([Hyp])[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111862	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111863	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m

	(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111864	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111865	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112336	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112337	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112338	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112339	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112340	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(C)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112341	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](

0112342	G)[Ssp].[moe](G)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112343	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112344	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112345	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](C)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112346	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].d([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112347	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112348	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112349	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112350	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0112351	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112352	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112353	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112354	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].m([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112355	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112356	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112357	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112358	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](C)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112359	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].d([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112360	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112361	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](A)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112362	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(U)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112363	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(U)[Ssp].[fl2r](C)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112364	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](C)[Ssp].[moe]([m5C])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112365	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe]([m5C])p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112366	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112367	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112368	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m

	(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112369	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112370	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112371	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(C)p.[fl2r](A)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112372	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112373	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](U)[n001R].m(C)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112374	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](U)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112375	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112376	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(U)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112377	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp

	].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112378	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112379	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112381	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(G)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112382	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(G)[Ssp].[fl2r]([Hyp])[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112384	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m([Hyp])p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112385	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112387	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].m(U)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112388	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(U)[Ssp].[fl2r]([Hyp])[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112389	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r]([Hyp])[n001

	R].m([Hyp])p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112391	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r]([Hyp])[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112392	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m([Hyp])p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112393	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m([Hyp])p.[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112394	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112395	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112396	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r]([Hyp])[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112398	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r]([Hyp])[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111802	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2

0111818	r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111820	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111846	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112336	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112337	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112338	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112339	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112340	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(C)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112341	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0112342	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112343	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112344	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112345	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](C)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112346	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].d([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112347	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].m([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112348	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112349	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112350	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-

	1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112351	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112352	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112353	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112354	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].m([3nU])[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112355	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112356	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.d([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112357	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.m([3nU])[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112358	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](C)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112359	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].d([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(

	G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112360	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].m([3nU])[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112361	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](A)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112362	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(U)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112363	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(U)[Ssp].[fl2r](C)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112364	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](C)[Ssp].[moe]([m5C])p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112365	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe]([m5C])p.[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112366	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112367	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](U)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112368	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](U)[Ssp].m(G)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp

	].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112369	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(G)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112370	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112371	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(C)p.[fl2r](A)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112372	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112373	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](U)[n001R].m(C)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112374	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(C)p.[fl2r](U)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112375	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](U)[Ssp].m(U)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112376	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(U)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112377	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m

	(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112378	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112379	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112381	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(G)[Ssp].m(G)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112382	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(G)[Ssp].[fl2r]([Hyp])[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112384	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].m([Hyp])p.[fl2r](U)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112385	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112387	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](G)[Ssp].m(U)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112388	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(U)[Ssp].[fl2r]([Hyp])[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](

0112389	G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r]([Hyp])[n001R].m([Hyp])p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112391	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r]([Hyp])[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112392	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m([Hyp])p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112393	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m([Hyp])p.[fl2r](G)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112394	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](G)[Ssp].m(G)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112395	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(G)p.[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112396	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](G)[Ssp].[fl2r]([Hyp])[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112398	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r]([Hyp])[Ssp].[fl2r](U)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111862	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

ADR-0111863	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111864	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].d([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0111865	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nT])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112416	RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[n006R].m([3nU])[n006R].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0
ADR-0112411	RNA1{p.[moe](G)[n006R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n006R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n006R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n006R].m(A)p.[fl2r](A)[Ssp].m(G)[n006R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

Table 1 and Table 1A (Continued): Certain Useful Base Sequences
GGAUAAGGCCACUGUGGAAAGGCAUGAAGC;
GGAUAAGGCCACUGUAGAAAGGCAUGAAGC;
GGAUTAGGCCACUGUAGAAAGGCAUGAAGC;
GGAUAAGGUCACUGUAGAAAGGCAUGAAGC;
GGAUUAGGCCACUGUAGAAAGGCAUGAAGC;
GGAUTAGGUCACUGUAGAAAGGCAUGAAGC;
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GGAUAAGGUCACUGUGGAAAGGCAUGAAGC;
GGAUTAGGUCACUGUGGAAAGGCAUGAAGC;
GGAUCAGGCCACUGUAGAAAGGCAUGAAGC;
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GGAUAAGGCCACUGUCGAAAGGCAUGAAGC;
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GGAUTUGGCCACUGUAGAAAGGCAUGAAGC;
GGAUAUCGCCACUGUAGAAAGGCAUGAAGC;
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GGAGAAGGCCACUGUAGAAAGGCA[3nU]GAAGC;
GGAUGAGGCCACUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCUACUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCGCUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCAUUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGGAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAGAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAAAGGCG[3nU]GAAGC;
GGAUAAGGCCACUGUAGAAAGGC[Hyp][3nU]GAAGC;
GGAUAAGGCCACUGUAGAAAGGC[purine][3nU]GAAGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU]GAAG[m5C];
GATAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
ATAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
TAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
AAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAAAGGCA[3nU]GAAG[m5C];
GGATAAGGCCACUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGG[m5C]CACUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGC[m5C]ACUGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCA[m5C]UGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACTGUAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGTAGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAAAGG[m5C]A[3nU]GAAGC;
GGGUAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUGAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAGGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCUACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCGCUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCAUUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGGAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAGAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAAGGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAAAGGUA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAAAGGCG[3nU]GAAGC;

GGAUAAGGCCACUGUGGAAAGGCA[3nU]GGAGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU]GAGGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU]GAAGU;
GGAUAAGGCCA[m5C]TGUGGAAAGGCA[3nU]GAAGC;
GGATAAGGCCACUGUGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGTGGAAAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU][Hyp]AAGC;
GGAUAAGGCCACUGUGGAAAGGCA[3nU]GAAGCA;
GGAUAAGGCCACUGUAGAAGGGGA[3nU]GAAGC;
GGGACACGGUGAUGGAGAAGGGCA[3nU]GAAGC;
AUAAGGCCACUGUAGAAGGGGA[3nU]GAAGCAG;
GGGAUAAGGCCACUGAGAAGGGGA[3nU]GAAGC;
AGGGAUAAGGCCACUAGAAGGGGA[3nU]GAAGC;
AGGAGGGAUAAGGCCAGAAGGGGA[3nU]GAAGC;
GAUAAGGCCACUGUAGAAGGGCA[3nU]GAAGCA;
AUAAGGCCACUGUAGAAGGGCA[3nU]GAAGCAG;
GGGAUAAGGCCACUGAGAAGGGCA[3nU]GAAGC;
AGGGAUAAGGCCACUAGAAGGGCA[3nU]GAAGC;
AGGAGGGAUAAGGCCAGAAGGGCA[3nU]GAAGC;
GAUAA[m5C]GCCACUGUAGAAAG[m5C]CA[3nU]GAAGCA;
GAUAA[m5C]GCCTCUGUAGAAAG[m5C]CA[3nU]GAAGCA;
AUAAGGCCACUGUAGAAAGGCA[3nU]GAAGCAG;
UAAGGCCACUGUAGAAAGGCA[3nU]GAAGCAGG;
AAGGCCACUGUAGAAAGGCA[3nU]GAAGCAGGA;
GGAUAAGGCCACUGUGGGGAGGCA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAAGGGUA[3nU]GAAGC;
GGAUAAGGCCACUGUAGAGAGGUA[3nU]GAAGC;
GGGAUAAGGCCACUGUAGAAAGGCA[3nU]GAAGCA;
GGAUAAGGCCACUGUAGAAAGGCA[3nU]GAAGCAG

Notes:

HELM Description and Base Sequence, due to their length, may be divided into multiple lines in Table 1 or Table 1A. Unless otherwise specified, all oligonucleotides in Table 1 and Table 1A are single-stranded. As appreciated by those skilled in the art, nucleoside units are unmodified and contain unmodified nucleobases and 2`-deoxy sugars unless otherwise indicated (e.g., with m, [fl2r], etc.); linkages, unless otherwise indicated, are natural phosphate linkages; and acidic/basic groups may independently exist in their salt forms. If a sugar is not specified, the sugar is a natural DNA sugar; and if an internucleotidic linkage is not specified, the internucleotidic linkage is a natural phosphate linkage. A natural DNA sugar may also be indicated with "d" as in d(G), d(A), d(C), d(T), etc., and a natural phosphate linkage may be indicated with "p" in Table 1 or Table 1A. Oligonucleotides in Table 1 and Table 1A are described using various features of the Hierarchical Editing Language for Macromolecules (HELM), which is described in, e.g., Zhang, T. et al. J Chem Inf Model. 2012 Oct 22;52(10):2796-806 and Milton, J. et al. J Chem Inf Model. 2017 Jun 26;57(6):1233-1239. As described in Zhang et al., 2012 and Milton et al., 2017, connections between oligonucleotides, linker moieties, GalNAc moieties, etc. may be indicated in HELM, for example, as the following: CHEM1,RNA1,1:R1-1:R1, wherein CHEM1 is, e.g., a first linker or moiety, RNA1 is an oligonucleotide, and 1:R1-1:R1 indicates that CHEM1 is linked via a first attachment point to a first

attachment point on a first monomer of RNA1, as described herein (see, e.g., below).

Moieties and modifications:

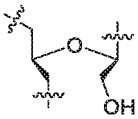
m: 2'-OMe (sugar is 2'-*O*-methylribose);

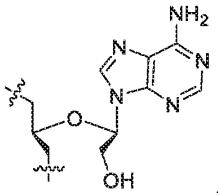
[m5C]: methyl at 5-position of C (nucleobase is 5-methylcytosine);

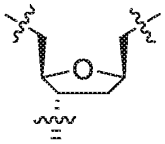
[fl2r]: 2'-F (sugar is 2'-fluoro-2'-deoxyribose);

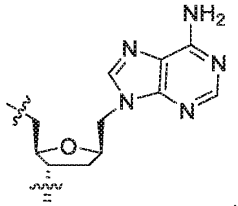
[moe]: 2'-MOE (2'−$OCH_2CH_2OCH_3$; sugar is 2'-*O*-methoxyethylribose);

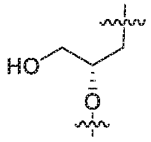
[moe]([m5C]): 5-methyl 2'-O-methoxyethyl C;

[una]: a UNA sugar of structure . As those skilled in the art reading the present disclosure appreciate, in Table 1 and Table 1A, the top left carbon atom with a connection site corresponds to the 5'-carbon of a ribose and the bottom left carbon atom with a connection site corresponds to the 3'-carbon of a ribose. In various oligonucleotides, such carbon atoms are bonded to oxygen atoms that are bonded to linkage phosphorus atoms. Those skilled in the art reading the present disclosure also appreciate that the carbon atom on the right with a connection site is bonded to a nucleobase;

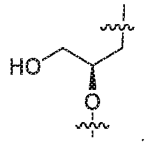
[una](A): . See also [una] above;

[m1d]: . As those skilled in the art reading the present disclosure appreciate, in Table 1 and Table 1A, the top left carbon atom with a connection site corresponds to the 5'-carbon of a ribose and the bottom left carbon atom with a connection site corresponds to the 3'-carbon of a ribose. In various oligonucleotides, such carbon atoms are bonded to oxygen atoms that are bonded to linkage phosphorus atoms. Those skilled in the art reading the present disclosure also appreciate that the carbon atom on the right with a connection site is bonded to a nucleobase;

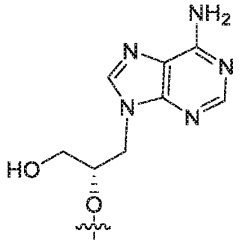
[m1d](A): . See also [m1d] above. [m1d] may also be combined with other nucleobases, e.g., in [m1d](G), [m1d](T), [m1d](C);



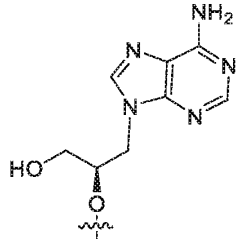
[Sgna]: . As those skilled in the art reading the present disclosure appreciate, in Table 1 and Table 1A, the hydroxyl group corresponds to the 5'-hydroxyl group of a ribose and the oxygen atom with a connection site corresponds to the 3'-oxygen of a ribose. In various oligonucleotides, the oxygen atom in the hydroxyl group and the oxygen atom with a connection site are bonded to linkage phosphorus atoms. Those skilled in the art reading the present disclosure also appreciate that the carbon atom on the right with a connection site is bonded to a nucleobase;



[Rgna]: . As those skilled in the art reading the present disclosure appreciate, in Table 1 and Table 1A, the hydroxyl group corresponds to the 5'-hydroxyl group of a ribose and the oxygen atom with a connection site corresponds to the 3'-oxygen of a ribose. In various oligonucleotides, the oxygen atom in the hydroxyl group and the oxygen atom with a connection site are bonded to linkage phosphorus atoms. Those skilled in the art reading the present disclosure also appreciate that the carbon atom on the right with a connection site is bonded to a nucleobase;



[Sgna](A): . See also [Sgna] above. [Sgna] may also be combined with other nucleobases, e.g., in [Sgna](G);



[Rgna](A): . See also [Rgna] above;

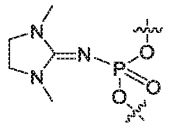
p: phosphodiester (phosphate). It can be a linkage or be an end group (or a component thereof), e.g., a linkage between a linker and an oligonucleotide chain, an internucleotidic linkage (a natural phosphate linkage), etc.; if no linkage is indicated in the Description column, it is typically a phosphodiester unless otherwise indicated;

[sp]: phosphorothioate. It can be an end group, or a linkage, e.g., a linkage between linker and an

oligonucleotide chain, an internucleotidic linkage (a phosphorothioate internucleotidic linkage), etc.;

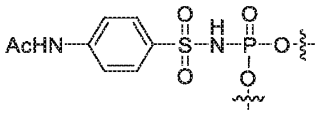
[Rsp]: phosphorothioate in the *R*p configuration;

[Ssp]: phosphorothioate in the *S*p configuration;

n001 or [n001]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

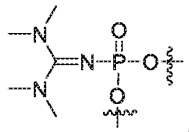
[n001R]: n001 in Rp configuration;

[n001S]: n001 in Sp configuration;

n006: . Those skilled in the art reading the present disclosure appreciate that in Table 1, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

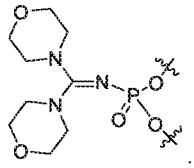
[n006R]: n006 in Rp configuration;

[n006S]: n006 in Sp configuration;

n003 or [n003]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

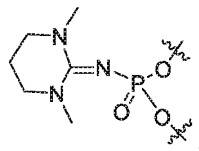
[n003R]: n003 in Rp configuration;

[n003S]: n003 in Sp configuration;

n008 or [n008]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

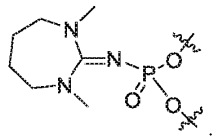
[n008R]: n008 in Rp configuration;

[n008S]: n008 in Sp configuration;

n025 or [n025]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

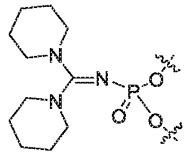
[n025R]: n025 in Rp configuration;

[n025S]: n025 in Sp configuration;

n026 or [n026]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

[n026R]: n026 in Rp configuration;

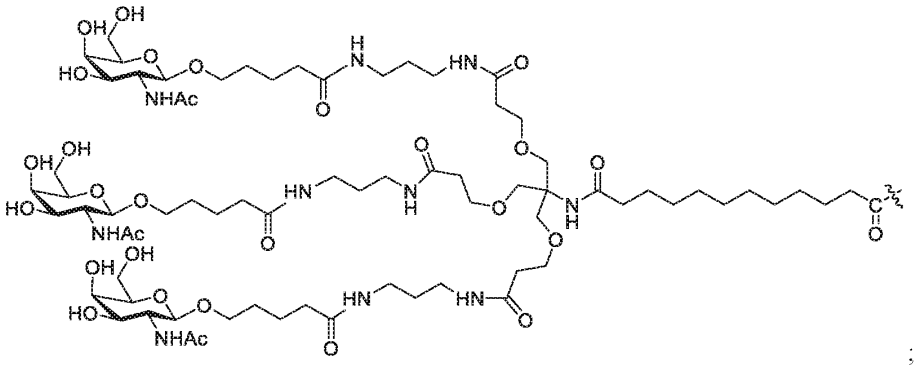
[n026S]: n026 in Sp configuration;

n0078 or [n0078]: . Those skilled in the art reading the present disclosure appreciate that in Table 1 and Table 1A, the oxygen atoms are bonded as the corresponding oxygen atoms in phosphodiester linkages (e.g., to a 5'-carbon atom of a sugar and to a 3'-carbon of a sugar);

[n0078R]: n0078 in Rp configuration;

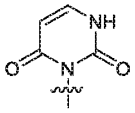
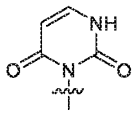
[n0078S]: n0078 in Sp configuration;

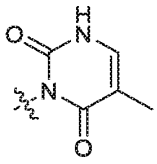
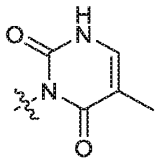
Mod001, GalNAc3C12oyl or [GalNAc3C12oyl]:

;

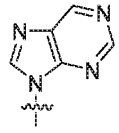
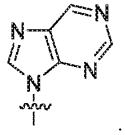
L001, nC6o or [nC6o]: $-NH-(CH_2)_6-$ linker (C6 linker, C6 amine linker or C6 amino linker), connected to Mod or CHEM (e.g., Mod001 or [GalNAc3C12oyl]) through –NH– (e.g., forming an amide group

−C(O)−NH−), and, in various cases, the 5'-end of the oligonucleotide chain through a phosphate linkage (p, O or PO; those skilled in the art appreciate that in the case of a phosphate linkage, the end $-CH_2-$ is bonded to an oxygen atom which is bonded to linkage phosphorus). Those skilled in the art appreciate that [nC6o] may also be properly considered as 6-aminohexanol wherein, as indicated, its amino group forms an amide (e.g., the nitrogen of the amino group is bonded to −C(O)− of [GalNAc3C12oyl]) and its hydroxyl forms a linkage such as a phosphate linkage (e.g., the oxygen of the hydroxyl group is boned to the linkage phosphorus of a phosphate linkage);

[3nU]: a nucleoside whose base is . For example, m([3nU]) indicates the presence of a nucleoside whose sugar is 2'-*O*-methylribose and whose nucleobase is ;

[3nT]: a nucleoside whose base is . For example, m([3nT]) indicates the presence of a nucleoside whose sugar is 2'-*O*-methylribose and whose nucleobase is ;

[Hyp]: a nucleoside whose base is hypoxanthine. For example, d([Hyp]) indicates the presence of a nucleoside whose sugar is 2'-deoxyribose and whose nucleobase is hypoxanthine;

[purine]: a nucleoside whose base is . For example, d([purine]) indicates the presence of a nucleoside whose sugar is 2'-deoxyribose and whose nucleobase is .

In some embodiments, a sugar is bonded to an internucleotidic linkage through an oxygen atom, e.g., as in typical natural DNA molecules. In some embodiments, a sugar is bonded to an internucleotidic linkage through an atom that is not oxygen. In some embodiments, a sugar is bonded to an internucleotidic linkage through a nitrogen atom of a sugar. In some embodiments, a sugar is bonded to an internucleotidic linkage through a ring nitrogen atom of a sugar; in such cases, a ring nitrogen atom of a sugar may directly form a bond with a

linkage phosphorus atom, and those skilled in the art will appreciate an oxygen atom may be removed from a linkage. Certain reagents (e.g., phosphoramidites, nucleosides, etc.) and methods for utilizing various modifications, e.g., those exemplified in the Tables herein, such as modified sugars, modified nucleobases, etc., are described in the Examples, WO 2021/071858 or WO 2022/099159, the modified sugars, modified nucleobases and modified internucleotidic linkages of each of which are independently incorporated herein by reference. *Oligonucleotide Compositions*

[00639] Among other things, the present disclosure provides various oligonucleotide compositions. In some embodiments, the present disclosure provides oligonucleotide compositions of oligonucleotides described herein. In some embodiments, an oligonucleotide composition comprises a plurality of oligonucleotides described in the present disclosure. In some embodiments, an oligonucleotide composition is chirally controlled. In some embodiments, an oligonucleotide composition is not chirally controlled (stereorandom).

[00640] Linkage phosphorus of natural phosphate linkages is achiral. Linkage phosphorus of many modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages, are chiral. In some embodiments, during preparation of oligonucleotide compositions (e.g., in traditional phosphoramidite oligonucleotide synthesis), configurations of chiral linkage phosphorus are not purposefully designed or controlled, creating non-chirally controlled (stereorandom) oligonucleotide compositions (substantially racemic preparations) which are complex, random mixtures of various stereoisomers (diastereoisomers) - for oligonucleotides with n chiral internucleotidic linkages (linkage phosphorus being chiral), typically 2n stereoisomers (e.g., when n is 10, 2^10 =1,032; when n is 20, 2^20 = 1,048,576). These stereoisomers have the same constitution, but differ with respect to the pattern of stereochemistry of their linkage phosphorus.

[00641] In some embodiments, stereorandom oligonucleotide compositions have sufficient properties and/or activities for certain purposes and/or applications. In some embodiments, stereorandom oligonucleotide compositions can be cheaper, easier and/or simpler to produce than chirally controlled oligonucleotide compositions. However, stereoisomers within stereorandom compositions may have different properties, activities, and/or toxicities, resulting in inconsistent therapeutic effects and/or unintended side effects by stereorandom compositions, particularly compared to certain chirally controlled oligonucleotide compositions of oligonucleotides of the same constitution.

[00642] In some embodiments, the present disclosure encompasses technologies for designing and preparing chirally controlled oligonucleotide compositions. In some embodiments, the present disclosure provides chirally controlled oligonucleotide compositions, e.g., of many oligonucleotides in Table 1 and Table 1A which contain S and/or R in their stereochemistry/linkage. In some embodiments, a chirally controlled oligonucleotide composition comprises a controlled/pre-determined (not random as in stereorandom compositions) level of a plurality of oligonucleotides, wherein the oligonucleotides share the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled internucleotidic linkages). In some embodiments, the oligonucleotides share the same pattern of backbone chiral centers

(stereochemistry of linkage phosphorus). In some embodiments, a pattern of backbone chiral centers is as described in the present disclosure. In some embodiments, oligonucleotides of a plurality are structural identical.

[00643] In some embodiments, the present disclosure provides an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages").

[00644] In some embodiments, the present disclosure provides an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence, for oligonucleotides of the plurality.

[00645] In some embodiments, an oligonucleotide composition is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common pattern of backbone linkages, and

the same linkage phosphorus stereochemistry at one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more) chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence and pattern of backbone linkages, for oligonucleotides of the plurality.

[00646] In some embodiments, an oligonucleotide composition is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common patter of backbone linkages, and

a common pattern of backbone chiral centers, which pattern comprises at least one Sp,

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence and pattern of backbone linkages, for oligonucleotides of the plurality.

[00647] In some embodiments, an oligonucleotide composition is a chirally controlled oligonucleotide

composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common patter of backbone linkages, and

a common pattern of backbone chiral centers, which pattern comprises at least one Rp,

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence and pattern of backbone linkages, for oligonucleotides of the plurality.

[00648] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

1) a common constitution, and

2) share the same linkage phosphorus stereochemistry at one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more) chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides of the common constitution, for oligonucleotides of the plurality.

[00649] In some embodiments, the present disclosure provides an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein stereochemical purity of the linkage phosphorus of each chirally controlled internucleotidic linkage is independently 80%-100% (e.g., 85-100%, 90-100%, about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%).

[00650] In some embodiments, an oligonucleotide composition is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common pattern of backbone linkages, and

the same linkage phosphorus stereochemistry at one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more) chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein stereochemical purity of the linkage phosphorus of each chirally controlled internucleotidic linkage is independently 80%-100% (e.g., 85-100%, 90-100%, about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%).

[00651] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

1) a common constitution, and

2) share the same linkage phosphorus stereochemistry at one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more) chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein stereochemical purity of the linkage phosphorus of each chirally controlled internucleotidic linkage is independently 80%-100% (e.g., 85-100%, 90-100%, about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5%).

[00652] In some embodiments, the present disclosure provides an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein the common base sequence is complementary to a base sequence of a portion of a nucleic acid which portion comprises a target adenosine.

[00653] In some embodiments, the present disclosure provides an oligonucleotide composition comprising one or more pluralities of oligonucleotides, wherein oligonucleotides of each plurality independently share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein the common base sequence of each plurality is independently complementary to a base sequence of a portion of a nucleic acid which portion comprises a target adenosine.

[00654] In some embodiments, the present disclosure provides an composition comprising a plurality of oligonucleotides which are of a particular oligonucleotide type characterized by:

a) a common base sequence;

b) a common pattern of backbone linkages;

c) a common pattern of backbone chiral centers;

d) a common pattern of backbone phosphorus modifications;

which composition is chirally controlled in that it is enriched, relative to a substantially racemic preparation of oligonucleotides having the same common base sequence, pattern of backbone linkages and pattern of backbone phosphorus modifications, for oligonucleotides of the particular oligonucleotide type, or a non-random level of all oligonucleotides in the composition that share the common base sequence are oligonucleotides of the plurality; and

wherein the common base sequence is complementary to a base sequence of a portion of a nucleic acid which portion comprises a target adenosine.

[00655] In some embodiments, as described herein a portion can be about or at least about 10-40, 15-40, 20-40, e.g., 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, nucleobases long. In some embodiments, a portion is about or at least about or no more than about 1%-50% of a nucleic acid. In some embodiments, a portion is the whole length of a nucleic acid. In some embodiments, a common base sequence is complementary to a base sequence of a portion of a nucleic acid as described herein. In some embodiments, it is fully complementary across its length except at a nucleobase opposite to a target adenosine. In some embodiments, it is fully complementary across its length. In some embodiments, a target adenosine is associated with a condition, disorder or disease. In some embodiments, a target adenosine is edited to I by a provided oligonucleotide or composition. In some embodiments, as described herein editing increases expression, level and/or activity of a transcript or a product thereof (e.g., a mRNA, a protein, etc.). In some embodiments, as described herein editing reduces expression, level and/or activity of a transcript or a product thereof (e.g., a mRNA, a protein, etc.).

[00656] In some embodiments, oligonucleotide of a plurality share the same nucleobase modifications and/or sugar modifications. In some embodiments, oligonucleotide of a plurality share the same internucleotidic linkage modifications (wherein the internucleotidic linkages may be in various acid, base, and/or salt forms). In some embodiments, oligonucleotides of a plurality share the same nucleobase modifications, sugar modifications, and internucleotidic linkage modifications, if any. In some embodiments, oligonucleotides of a plurality are of the same form, e.g., an acid form, a base form, or a particularly salt form (e.g., a pharmaceutically acceptable salt form, e.g., salt form). In some embodiments, oligonucleotides in a composition may exist as one or more forms, e.g., acid forms, base forms, and/or one or more salt forms. In some embodiments, in an aqueous solution (e.g., when dissolved in a buffer like PBS), anions and cations may dissociate. In some embodiments, oligonucleotides of a plurality are of the same constitution. In some embodiments, oligonucleotides of a plurality are structurally identical. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides are of a common constitution, and share the same linkage phosphorus stereochemistry at one or more (e.g., 1-60, 1-50, 1-40, 1-30, 1-25, 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60 or more) chiral internucleotidic linkages (chirally controlled internucleotidic linkages), wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides of the common constitution, for oligonucleotides of the plurality.

[00657] In some embodiments, at least one chiral internucleotidic linkage is chirally controlled. In some embodiments, at least 2 internucleotidic linkages are independently chirally controlled. In some embodiments, the number of chirally controlled internucleotidic linkages is at least 3. In some embodiments, it is at least 4.

In some embodiments, it is at least 5. In some embodiments, it is at least 6. In some embodiments, it is at least 7. In some embodiments, it is at least 8. In some embodiments, it is at least 9. In some embodiments, it is at least 10. In some embodiments, it is at least 11. In some embodiments, it is at least 12. In some embodiments, it is at least 13. In some embodiments, it is at least 14. In some embodiments, it is at least 15. In some embodiments, it is at least 20. In some embodiments, it is at least 25. In some embodiments, it is at least 30.

[00658] In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all internucleotidic linkages are chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all chiral internucleotidic linkages are chirally controlled. In some embodiments, at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of all phosphorothioate internucleotidic linkages are chirally controlled. In some embodiments, a percentage is at least 50%. In some embodiments, a percentage is at least 60%. In some embodiments, a percentage is at least 70%. In some embodiments, a percentage is at least 80%. In some embodiments, a percentage is at least 90%. In some embodiments, a percentage is at least 90%. In some embodiments, each chiral internucleotidic linkage is chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage is chirally controlled.

[00659] In some embodiments, no more than 1-10, e.g., no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, chiral internucleotidic linkages are not chirally controlled. In some embodiments, no more than 1 chiral internucleotidic linkages is not chirally controlled. In some embodiments, no more than 2 chiral internucleotidic linkages are not chirally controlled. In some embodiments, no more than 3 chiral internucleotidic linkages are not chirally controlled. In some embodiments, no more than 4 chiral internucleotidic linkages are not chirally controlled. In some embodiments, no more than 5 chiral internucleotidic linkages are not chirally controlled. In some embodiments, the number of non-chirally

controlled internucleotidic linkages is 1. In some embodiments, it is 2. In some embodiments, it is 3. In some embodiments, it is 4. In some embodiments, it is 5.

[00660] In some embodiments, the present disclosure provides a composition comprising a plurality of oligonucleotides, wherein each oligonucleotide of the plurality is independently a particular oligonucleotide or a salt thereof. In some embodiments, the present disclosure provides a composition comprising a plurality of oligonucleotides, wherein each oligonucleotide of the plurality is independently a particular oligonucleotide or a pharmaceutically acceptable salt thereof. In some embodiments, such a composition is enriched relative to a substantially racemic preparation of a particular oligonucleotide. As appreciated by those skilled in the art, oligonucleotides of the plurality share a common sequence which is the base sequence of the particular oligonucleotide. In some embodiments, at least about 5%-100%, 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-100%, 5%-90%, 10%-90%, 20-90%, 30%-90%, 40%-90%, 50%-90%, 5%-85%, 10%-85%, 20-85%, 30%-85%, 40%-85%, 50%-85%, 5%-80%, 10%-80%, 20-80%, 30%-80%, 40%-80%, 50%-80%, 5%-75%, 10%-75%, 20-75%, 30%-75%, 40%-75%, 50%-75%, 5%-70%, 10%-70%, 20-70%, 30%-70%, 40%-70%, 50%-70%, 5%-65%, 10%-65%, 20-65%, 30%-65%, 40%-65%, 50%-65%, 5%-60%, 10%-60%, 20-60%, 30%-60%, 40%-60%, 50%-60%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of all oligonucleotides in the composition that share the base sequence of a the particular oligonucleotide are oligonucleotide of the plurality. In some embodiments, at least about 5%-100%, 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-100%, 5%-90%, 10%-90%, 20-90%, 30%-90%, 40%-90%, 50%-90%, 5%-85%, 10%-85%, 20-85%, 30%-85%, 40%-85%, 50%-85%, 5%-80%, 10%-80%, 20-80%, 30%-80%, 40%-80%, 50%-80%, 5%-75%, 10%-75%, 20-75%, 30%-75%, 40%-75%, 50%-75%, 5%-70%, 10%-70%, 20-70%, 30%-70%, 40%-70%, 50%-70%, 5%-65%, 10%-65%, 20-65%, 30%-65%, 40%-65%, 50%-65%, 5%-60%, 10%-60%, 20-60%, 30%-60%, 40%-60%, 50%-60%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of all oligonucleotides in the composition that share the constitution of the particular oligonucleotide or a salt thereof are oligonucleotide of the plurality. In some embodiments, a percentage is at least 10%. In some embodiments, a percentage is at least 20%. In some embodiments, a percentage is at least 30%. In some embodiments, a percentage is at least 40%. In some embodiments, a percentage is at least 50%. In some embodiments, it is at least 60%. In some embodiments, it is at least 70%. In some embodiments, it is at least 80%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%. In some embodiments, it is about 5-100%. In some embodiments, it is about 10-100%. In some embodiments, it is about 20-100%. In some embodiments, it is about 30-90%. In some embodiments, it is about 30-80%. In some embodiments, it is about 30-70%. In some embodiments, it is about 40-90%. In some embodiments, it is about 40-80%. In some embodiments, it is about 40-70%. In some embodiments, a particular oligonucleotide is an oligonucleotide exemplified herein, e.g., an oligonucleotide of Table 1, Table 1A, or another table.

[00661] In some embodiments, an enrichment relative to a substantially racemic preparation is that at least about 5%-100%, 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-100%, 5%-90%, 10%-90%, 20-90%,

30%-90%, 40%-90%, 50%-90%, 5%-85%, 10%-85%, 20-85%, 30%-85%, 40%-85%, 50%-85%, 5%-80%, 10%-80%, 20-80%, 30%-80%, 40%-80%, 50%-80%, 5%-75%, 10%-75%, 20-75%, 30%-75%, 40%-75%, 50%-75%, 5%-70%, 10%-70%, 20-70%, 30%-70%, 40%-70%, 50%-70%, 5%-65%, 10%-65%, 20-65%, 30%-65%, 40%-65%, 50%-65%, 5%-60%, 10%-60%, 20-60%, 30%-60%, 40%-60%, 50%-60%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of all oligonucleotides in the composition, or all oligonucleotides in the composition that share the common base sequence of a plurality, or all oligonucleotides in the composition that share the common constitution of a plurality, are oligonucleotide of the plurality. In some embodiments, a percentage is at least 10%. In some embodiments, a percentage is at least 20%. In some embodiments, a percentage is at least 30%. In some embodiments, a percentage is at least 40%. In some embodiments, a percentage is at least 50%. In some embodiments, it is at least 60%. In some embodiments, it is at least 70%. In some embodiments, it is at least 80%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%. In some embodiments, it is about 5-100%. In some embodiments, it is about 10-100%. In some embodiments, it is about 20-100%. In some embodiments, it is about 30-90%. In some embodiments, it is about 30-80%. In some embodiments, it is about 30-70%. In some embodiments, it is about 40-90%. In some embodiments, it is about 40-80%. In some embodiments, it is about 40-70%.

[00662] In some embodiments, at least about 5%-100%, 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-100%, 5%-90%, 10%-90%, 20-90%, 30%-90%, 40%-90%, 50%-90%, 5%-85%, 10%-85%, 20-85%, 30%-85%, 40%-85%, 50%-85%, 5%-80%, 10%-80%, 20-80%, 30%-80%, 40%-80%, 50%-80%, 5%-75%, 10%-75%, 20-75%, 30%-75%, 40%-75%, 50%-75%, 5%-70%, 10%-70%, 20-70%, 30%-70%, 40%-70%, 50%-70%, 5%-65%, 10%-65%, 20-65%, 30%-65%, 40%-65%, 50%-65%, 5%-60%, 10%-60%, 20-60%, 30%-60%, 40%-60%, 50%-60%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% of all oligonucleotides in the composition that share the common base sequence of a plurality are oligonucleotide of the plurality. In some embodiments, a percentage is at least 10%. In some embodiments, a percentage is at least 20%. In some embodiments, a percentage is at least 30%. In some embodiments, a percentage is at least 40%. In some embodiments, a percentage is at least 50%. In some embodiments, it is at least 60%. In some embodiments, it is at least 70%. In some embodiments, it is at least 80%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%. In some embodiments, it is about 5-100%. In some embodiments, it is about 10-100%. In some embodiments, it is about 20-100%. In some embodiments, it is about 30-90%. In some embodiments, it is about 30-80%. In some embodiments, it is about 30-70%. In some embodiments, it is about 40-90%. In some embodiments, it is about 40-80%. In some embodiments, it is about 40-70%.

[00663] Levels of oligonucleotides of a plurality in chirally controlled oligonucleotide compositions are controlled. In contrast, in non-chirally controlled (or stereorandom, racemic) oligonucleotide compositions (or preparations), levels of oligonucleotides are random and not controlled. In some embodiments, an enrichment relative to a substantially racemic preparation is a level described herein.

[00664] In some embodiments, a level as a percentage (e.g., a controlled level, a pre-determined level, an enrichment) is or is at least $(DS)^{nc}$, wherein DS (diastereopurity of an individual internucleotidic linkage) is 90%-100%, and nc is the number of chiral linkage phosphorus as described in the present disclosure (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more). In some embodiments, a level as a percentage (e.g., a controlled level, a pre-determined level, an enrichment) is or is at least $(DS)^{nc}$, wherein DS (diastereopurity of an individual internucleotidic linkage) is 90%-100%, and nc is the number of chirally controlled internucleotidic linkages as described in the present disclosure (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more). In some embodiments, each chiral internucleotidic linkage is chirally controlled, and nc is the number of chiral internucleotidic linkage. In some embodiments, DS is 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more. In some embodiments, DS is or is at least 90%. In some embodiments, DS is or is at least 91%. In some embodiments, DS is or is at least 92%. In some embodiments, DS is or is at least 93%. In some embodiments, DS is or is at least 94%. In some embodiments, DS is or is at least 95%. In some embodiments, DS is or is at least 96%. In some embodiments, DS is or is at least 97%. In some embodiments, DS is or is at least 98%. In some embodiments, DS is or is at least 99%. In some embodiments, a level (e.g., a controlled level, a pre-determined level, an enrichment) is a percentage of all oligonucleotides in a composition that share the same constitution, wherein the percentage is or is at least $(DS)^{nc}$. For example, when DS is 99% and nc is 10, the percentage is or is at least 90% ($(99\%)^{10} \approx 0.90 = 90\%$). As appreciated by those skilled in the art, in a stereorandom preparation the percentage is typically about $1/2^{nc}$ - when nc is 10, the percentage is about $1/2^{10} \approx 0.001 = 0.1\%$. In some embodiments, an enrichment (e.g., relative to a substantially racemic preparation), a level, etc., is that at least about $(DS)^{nc}$ of all oligonucleotides in the composition, or all oligonucleotides in the composition that share the common base sequence of a plurality, or all oligonucleotides in the composition that share the common constitution of a plurality, are oligonucleotide of the plurality. In some embodiments, it is of all oligonucleotides in the composition. In some embodiments, it is of all oligonucleotides in the composition that share the common base sequence of a plurality. In some embodiments, it is of all oligonucleotides in the composition that share the common constitution of a plurality. In some embodiments, various forms (e.g., various salt forms) of an oligonucleotide may be properly considered to have the same constitution.

[00665] In some embodiments, oligonucleotides comprise one or more (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) chirally controlled chiral internucleotidic linkages the diastereomeric excess (d.e.) of whose linkage phosphorus is independently about or at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%. In some embodiments, about or at least about 50%, 60%, 70%, 75%, 80%, 85%, 90%, or 95% of all chiral internucleotidic linkages comprising a chiral linkage phosphorus are independently such a chirally controlled internucleotidic linkage. In some embodiments, about or at least about 50%, 60%, 70%, 75%, 80%, 85%, 90%, or 95% of phosphorothioate internucleotidic linkages are independently such a chirally controlled internucleotidic linkage. In some embodiments, each

phosphorothioate internucleotidic linkage is independently such a chirally controlled internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage comprising a chiral linkage phosphorus is independently such a chirally controlled internucleotidic linkage. In some embodiments, d.e. is about or at least about 80%. In some embodiments, d.e. is about or at least about 85%. In some embodiments, d.e. is about or at least about 90%. In some embodiments, d.e. is about or at least about 95%. In some embodiments, d.e. is about or at least about 96%. In some embodiments, d.e. is about or at least about 97%. In some embodiments, d.e. is about or at least about 98%.

[00666] In some embodiments, an oligonucleotide composition (also referred to as an oligonucleotide composition) is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common pattern of backbone linkages, and

the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the percentage of the oligonucleotides of the plurality within all oligonucleotides in the composition that share the common base sequence and pattern of backbone linkages is at least $(DS)^{nc}$, wherein DS is 90%-100%, and nc is the number of chiral linkage phosphorus.

[00667] In some embodiments, an oligonucleotide composition (also referred to as an oligonucleotide composition) is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common pattern of backbone linkages, and

the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the percentage of the oligonucleotides of the plurality within all oligonucleotides in the composition that share the common base sequence and pattern of backbone linkages is at least $(DS)^{nc}$, wherein DS is 90%-100%, and nc is the number of chirally controlled internucleotidic linkages.

[00668] In some embodiments, an oligonucleotide composition (also referred to as an oligonucleotide composition) is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common patter of backbone linkages, and

a common pattern of backbone chiral centers, which pattern comprises at least one *Sp*,

wherein the percentage of the oligonucleotides of the plurality within all oligonucleotides in the composition that share the common base sequence and pattern of backbone linkages is at least $(DS)^{nc}$, wherein DS is 90%-100%, and nc is the number of chiral linkage phosphorus.

[00669] In some embodiments, an oligonucleotide composition (also referred to as an oligonucleotide composition) is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence,

a common patter of backbone linkages, and

a common pattern of backbone chiral centers, which pattern comprises at least one *Sp*,

wherein the percentage of the oligonucleotides of the plurality within all oligonucleotides in the composition that share the common base sequence and pattern of backbone linkages is at least $(DS)^{nc}$, wherein DS is 90%-100%, and nc is the number of chirally controlled internucleotidic linkages.

[00670] In some embodiments, level of a diastereopurity of a plurality of oligonucleotides in a composition can be determined as the product of the diastereopurity of each chirally controlled internucleotidic linkage in the oligonucleotides. In some embodiments, diastereopurity of an internucleotidic linkage connecting two nucleosides in an oligonucleotide (or nucleic acid) is represented by the diastereopurity of an internucleotidic linkage of a dimer connecting the same two nucleosides, wherein the dimer is prepared using comparable conditions, in some instances, identical synthetic cycle conditions (e.g., for the linkage between Nx and Ny in an oligonucleotide ….NxNy….., the dimer is NxNy).

[00671] In some embodiments, a chirally controlled oligonucleotide composition comprises two or more pluralities of oligonucleotides, wherein each plurality is independently a plurality of oligonucleotides as described herein (e.g., in various chirally controlled oligonucleotide compositions). For example, in some embodiments, each plurality independently shares a common base sequence, and the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages, and each plurality is independently enriched compared to stereorandom preparation of that plurality or each plurality is independently of a level as described herein. In some embodiments, at least two pluralities or each plurality independently targets a different adenosine. In some embodiments, at least two pluralities or each plurality independently targets a different transcript of the same or different nucleic acids. In some embodiments, at least two pluralities or each plurality independently targets transcripts of a different gene. Among other things, such compositions may be utilized to target two or more targets, in some embodiments, simultaneously and in the same system.

[00672] In some embodiments, all chiral internucleotidic linkages are chiral controlled, and the composition is a completely chirally controlled oligonucleotide composition. In some embodiments, not all chiral internucleotidic linkages are chiral controlled internucleotidic linkages, and the composition is a partially chirally controlled oligonucleotide composition.

[00673] Oligonucleotides may comprise or consist of various patterns of backbone chiral centers (patterns of stereochemistry of chiral linkage phosphorus). Certain useful patterns of backbone chiral centers are described in the present disclosure. In some embodiments, a plurality of oligonucleotides share a common pattern of backbone chiral centers, which is or comprises a pattern described in the present disclosure (e.g., as in "Linkage Phosphorus Stereochemistry and Patterns Thereof", a pattern of backbone chiral centers of a

chirally controlled oligonucleotide in Table 1, Table 1A, etc.).

[00674] In some embodiments, a chirally controlled oligonucleotide composition is a chirally pure (or stereopure, stereochemically pure) oligonucleotide composition, wherein the oligonucleotide composition comprises a plurality of oligonucleotides, wherein the oligonucleotides are identical [including that each chiral element of the oligonucleotides, including each chiral linkage phosphorus, is independently defined (stereodefined)], and the composition does not contain other stereoisomers. A chirally pure (or stereopure, stereochemically pure) oligonucleotide composition of an oligonucleotide stereoisomer does not contain other stereoisomers (as appreciated by those skilled in the art, one or more unintended stereoisomers may exist as impurities).

[00675] Chirally controlled oligonucleotide compositions can demonstrate a number of advantages over stereorandom oligonucleotide compositions. Among other things, chirally controlled oligonucleotide compositions are more uniform than corresponding stereorandom oligonucleotide compositions with respect to oligonucleotide structures. By controlling stereochemistry, compositions of individual stereoisomers can be prepared and assessed, so that chirally controlled oligonucleotide composition of stereoisomers with desired properties and/or activities can be developed. In some embodiments, chirally controlled oligonucleotide compositions provides better delivery, stability, clearance, activity, selectivity, and/or toxicity profiles compared to, e.g., corresponding stereorandom oligonucleotide compositions. In some embodiments, chirally controlled oligonucleotide compositions provide better efficacy, fewer side effects, and/or more convenient and effective dosage regimens. Among other things, patterns of backbone chiral centers as described herein optionally combined with other structural features described herein, e.g., modifications of nucleobases, sugars, internucleotidic linkages, etc. can be utilized to provide to provide directed adenosine editing with high efficiency.

[00676] In some embodiments, an oligonucleotide composition comprises one or more internucleotidic linkages which are stereocontrolled (chirally controlled; in some embodiments, stereopure) and one or more internucleotidic linkages which are stereorandom. In some embodiments, an oligonucleotide composition comprises one or more internucleotidic linkages which are stereocontrolled (chirally controlled; in some embodiments, stereopure) and one or more internucleotidic linkages which are stereorandom.

[00677] In some embodiments, an oligonucleotide composition comprises one or more internucleotidic linkages which are stereocontrolled (e.g., chirally controlled or stereopure) and one or more internucleotidic linkages which are stereorandom. Such oligonucleotides may target various nucleic acids and may have various base sequences, and may provide efficient adenosine editing (e.g., conversion of A to I).

[00678] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition. In some embodiments, provided chirally controlled oligonucleotide compositions comprise a plurality of oligonucleotides of the same constitution, and have one or more internucleotidic linkages. In some embodiments, a plurality of oligonucleotides, e.g., in a chirally controlled oligonucleotide composition, is a plurality of an oligonucleotide selected from Table 1 or Table 1A (and/or one or more of various salts forms

thereof), wherein the oligonucleotide comprises at least one *R*p or *S*p linkage phosphorus in a chirally controlled internucleotidic linkage. In some embodiments, a plurality of oligonucleotides, e.g., in a chirally controlled oligonucleotide composition, is a plurality of an oligonucleotide selected from Table 1 or Table 1A (and/or one or more of various salts forms thereof), wherein each phosphorothioate internucleotidic linkage in the oligonucleotide is independently chirally controlled (each phosphorothioate internucleotidic linkage is independently *R*p or *S*p). In some embodiments, an oligonucleotide composition, e.g., an oligonucleotide composition is a substantially pure preparation of a single oligonucleotide in that oligonucleotides in the composition that are not the single oligonucleotide are impurities from the preparation process of the single oligonucleotide, in some case, after certain purification procedures. In some embodiments, a single oligonucleotide is an oligonucleotide of Table 1 or Table 1A, wherein each chiral internucleotidic linkage of the oligonucleotide is chirally controlled (e.g., indicated as S or R but not X in "Stereochemistry/Linkage").

[00679] In some embodiments, a chirally controlled oligonucleotide composition can have, relative to a corresponding stereorandom oligonucleotide composition, increased activity and/or stability, increased delivery, and/or decreased ability to elicit adverse effects such as complement, TLR9 activation, etc. In some embodiments, a stereorandom (non-chirally controlled) oligonucleotide composition differs from a chirally controlled oligonucleotide composition in that its corresponding plurality of oligonucleotides do not contain any chirally controlled internucleotidic linkages but the stereorandom oligonucleotide composition is otherwise identical to the chirally controlled oligonucleotide composition.

[00680] In some embodiments, the present disclosure pertains to a chirally controlled oligonucleotide composition which is capable of modulating level, activity or expression of a gene or a gene product thereof. In some embodiments, level, activity, or expression of a gene or a gene product thereof is increased (e.g., through conversion of A to I to introduce one or more G to A variations) as compared to a reference condition (e.g., absence of oligonucleotides and/or compositions of the present disclosure, and/or presence of a reference oligonucleotide and/or oligonucleotide composition (e.g., oligonucleotides of the same base sequence but different modifications, stereorandom compositions of oligonucleotides of comparable structures (e.g., base sequence, modifications, etc.) but lack of stereochemical control, etc.).

[00681] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is capable of increasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is, comprises, or comprises a span (e.g., at least 10 or 15 contiguous bases) of a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa). In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is capable of increasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is or comprises a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa). In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is

capable of increasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa).

[00682] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is capable of decreasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is, comprises, or comprises a span (e.g., at least 10 or 15 contiguous bases) of a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa). In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is capable of decreasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is or comprises a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa). In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition which is capable of decreasing the level, activity or expression of a gene or a gene product thereof, and comprises a plurality of oligonucleotides which share a common base sequence that is a base sequence disclosed herein (e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa).

[00683] In some embodiments, a provided chirally controlled oligonucleotide composition is a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotide. In some embodiments, a chirally controlled oligonucleotide composition is a chirally pure (or "stereochemically pure") oligonucleotide composition. In some embodiments, the present disclosure provides a chirally pure oligonucleotide composition of an oligonucleotide in Table 1 or Table 1A, wherein each chiral internucleotidic linkage of the oligonucleotide is independently chirally controlled (*Rp* or *Sp*, e.g., can be determined from R or S but not X in "Stereochemistry/Linkage"). As one of ordinary skill in the art will understand, chemical selectivity rarely, if ever, achieves completeness (absolute 100%). In some embodiments, a chirally pure oligonucleotide composition comprises a plurality of oligonucleotides, wherein oligonucleotides of the plurality are structurally identical and all have the same structure (the same stereoisomeric form; in the context of oligonucleotide, typically the same diastereomeric form as typically multiple chiral centers exist in an oligonucleotide), and the chirally pure oligonucleotide composition does not contain any other stereoisomers (in the context of oligonucleotide, typically diastereomers as typically multiple chiral centers exist in an oligonucleotide ; to the extent, e.g., achievable by stereoselective preparation). As appreciated by those skilled in the art, stereorandom (or "racemic", "non-chirally controlled") oligonucleotide compositions are random mixtures of many stereoisomers (e.g., 2^n diastereoisomers wherein n is the number of chiral linkage phosphorus for oligonucleotides in which other chiral centers (e.g., carbon chiral centers in sugars) are chirally controlled each independently existing in one configuration and only chiral linkage phosphorus centers are not chirally controlled).

[00684] Certain data showing properties and/or activities of chirally controlled oligonucleotide

composition, e.g., chirally controlled oligonucleotide composition in modulating level, activity and/or expression of target genes and/or products thereof, are shown in, for example, the Examples of this disclosure.

[00685] In some embodiments, the present disclosure provides an oligonucleotide composition comprising oligonucleotides that comprise at least one chiral linkage phosphorus. In some embodiments, the present disclosure provides an oligonucleotide composition comprising oligonucleotides that comprise at least one chiral linkage phosphorus. In some embodiments, the present disclosure provides an oligonucleotide composition in which the oligonucleotides comprise a chirally controlled phosphorothioate internucleotidic linkage, wherein the linkage phosphorus has a *R*p configuration. In some embodiments, the present disclosure provides an oligonucleotide composition in which the oligonucleotides comprise a chirally controlled phosphorothioate internucleotidic linkage, wherein the linkage phosphorus has a *S*p configuration. In some embodiments, the present disclosure provides an oligonucleotide composition in which the oligonucleotides comprise a chirally controlled phosphorothioate internucleotidic linkage, wherein the linkage phosphorus has a *R*p configuration and the linkage phosphorus has a *S*p configuration. In some embodiments, such oligonucleotide compositions are chirally controlled, and the *R*p and/or *S*p internucleotidic linkages are independently chirally controlled internucleotidic linkages.

[00686] In some embodiments, compared to reference oligonucleotides or oligonucleotide compositions, provided oligonucleotides or oligonucleotide compositions (e.g., chirally controlled oligonucleotide compositions) are surprisingly effective. In some embodiments, desired biological effects (e.g., as measured by increased (if increase is desired) and/or decreased (if decrease is desired) levels of mRNA, proteins, etc. whose levels are targeted for increase) can be enhanced by more than 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, or 100 fold (e.g., as measured by levels of desired mRNA, proteins, etc.). In some embodiments, a change is measured by increase of desired mRNA and/or protein levels, or decrease of undesired mRNA and/or protein levels, compared to a reference condition. In some embodiments, a change is measured by increase of a desired mRNA and/or protein level compared to a reference condition. In some embodiments, a change is measured by decrease of an undesired mRNA and/or level compared to a reference condition. In some embodiments, a reference condition is absence of provided oligonucleotides or oligonucleotide compositions, and or presence of reference oligonucleotides or oligonucleotide compositions, respectively. In some embodiments, a reference oligonucleotide shares the same base sequence, but different nucleobase modifications, sugar modifications, internucleotidic linkages modifications, and/or linkage phosphorus stereochemistry. In some embodiments, a reference oligonucleotide composition is a composition of oligonucleotides of the same base sequence, but different nucleobase modifications, sugar modifications, internucleotidic linkages modifications, and/or linkage phosphorus stereochemistry. In some embodiments, a reference composition for a chirally controlled oligonucleotide composition is a corresponding stereorandom composition of oligonucleotides having the same base sequence, nucleobase modifications, sugar modifications, and/or internucleotidic linkages modifications (but lack of and/or low levels of linkage phosphorus stereochemistry control), or having the same constitution.

[00687] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein the linkage phosphorus of at least one chirally controlled internucleotidic linkage is *Sp*. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein the majority of linkage phosphorus of chirally controlled internucleotidic linkages are *Sp*. In some embodiments, about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more, of all chirally controlled internucleotidic linkages (or of all chiral internucleotidic linkages, or of all internucleotidic linkages) are *Sp*. In some embodiments, about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more, of all chirally controlled phosphorothioate internucleotidic linkages are *Sp*. In some embodiments, no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of phosphorothioate internucleotidic linkages are non-chirally controlled or are chirally controlled and *Rp*. In some embodiments, no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 of phosphorothioate internucleotidic linkages are chirally controlled and *Rp*. In some embodiments, it is no more than 1. In some embodiments, it is no more than 2. In some embodiments, it is no more than 3. In some embodiments, it is no more than 4. In some embodiments, it is no more than 5. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein the majority of chiral internucleotidic linkages are chirally controlled and are *Sp* at their linkage phosphorus. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein each chiral internucleotidic linkage is chirally controlled and each chiral linkage phosphorus is *Sp*. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, e.g., chirally controlled oligonucleotide composition, wherein at least one chirally controlled internucleotidic linkage has a *Rp* linkage phosphorus. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein at least one chirally controlled internucleotidic linkage comprises a *Rp* linkage phosphorus and at least one chirally controlled internucleotidic linkage comprises a *Sp* linkage phosphorus.

[00688] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein at least two chirally controlled internucleotidic linkages have different linkage phosphorus stereochemistry and/or different P-modifications relative to one another, wherein a P-modification is a modification at a linkage phosphorus. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, wherein at least two chirally controlled internucleotidic linkages have different stereochemistry relative to one another, and the pattern of the backbone chiral centers of the oligonucleotides is characterized by a repeating pattern of alternating stereochemistry.

[00689] In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another. In certain

embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a natural phosphate linkage. In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a phosphorothioate internucleotidic linkage. In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a natural phosphate linkage and a phosphorothioate internucleotidic linkage. In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a phosphorothioate triester internucleotidic linkage. In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a natural phosphate linkage and a phosphorothioate triester internucleotidic linkage. In certain embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein with in each of the oligonucleotides at least two individual internucleotidic linkages have different P-modifications relative to one another, and each of the oligonucleotide comprises a phosphorothioate internucleotidic linkage and a phosphorothioate triester internucleotidic linkage.

[00690] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition, comprising a plurality of oligonucleotides which share a common base sequence that is the base sequence of an oligonucleotide disclosed herein, wherein at least one internucleotidic linkage is chirally controlled.

Linkage Phosphorus Stereochemistry and Pattern of Backbone Chiral Centers

[00691] Among other things, the present disclosure provides various oligonucleotide compositions. In some embodiments, the present disclosure provides oligonucleotide compositions of oligonucleotides described herein. In some embodiments, an oligonucleotide composition comprises a plurality of oligonucleotides described in the present disclosure. In some embodiments, an oligonucleotide composition is chirally controlled. In some embodiments, an oligonucleotide composition is not chirally controlled (stereorandom).

[00692] In contrast to natural phosphate linkages, linkage phosphorus of chiral modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages, are chiral. Among other things, the present

disclosure provides technologies (e.g., oligonucleotides, compositions, methods, etc.) comprising control of stereochemistry of chiral linkage phosphorus in chiral internucleotidic linkages. In some embodiments, as demonstrated herein, control of stereochemistry can provide improved properties and/or activities, including desired stability, reduced toxicity, improved modification of target nucleic acids, improved modulation of levels of transcripts and/or products (e.g., mRNA, proteins, etc.) encoded thereof, etc. In some embodiments, the present disclosure provides useful patterns of backbone chiral centers for oligonucleotides and/or regions thereof, which pattern includes a combination of stereochemistry of each chiral linkage phosphorus (*Rp* or *Sp*) of chiral linkage phosphorus, indication of each achiral linkage phosphorus (Op, if any), etc. from 5' to 3'. Certain patterns are provided in various Tables (e.g., Stereochemistry/Linkage as examples; such patterns can be applied to various oligonucleotides with various base sequences and modifications (e.g., those described herein including patterns thereof).

[00693] Useful patterns of backbone chiral centers, e.g., those for oligonucleotides, first domains, second domains, first subdomains, second subdomains, third subdomains, etc., are extensively described herein. For example, in some embodiments, high levels of *Sp* internucleotidic linkages of oligonucleotides or of one or more portions thereof (e.g., first domains, second domains, first subdomains, second subdomains, and/or third subdomains, and/or 5'-end portions and/or 3'-end portions therein) provide high stability and/or activities. In some embodiments, first domains contain high levels of *Sp* internucleotidic linkages. In some embodiments, second domains contain high levels of *Sp* internucleotidic linkages (in numbers and/or percentages, relative to natural phosphate linkages and/or *Rp* internucleotidic linkages). In some embodiments, first subdomains contain high levels of *Sp* internucleotidic linkages. In some embodiments, second subdomains contain high levels of *Sp* internucleotidic linkages. In some embodiments, third subdomains contain high levels of *Sp* internucleotidic linkages. In some embodiments, as demonstrated herein *Rp* internucleotidic linkages can be utilized in various locations and/or portions. For example, in some embodiments, first domains contain one or more or high levels of *Rp* internucleotidic linkages, and in some embodiments, second subdomains contain one or more or high levels of *Rp* internucleotidic linkages.

[00694] In some embodiments, a number of linkage phosphorus in chirally controlled internucleotidic linkages are *Sp*. In some embodiments, at least 10%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of chirally controlled internucleotidic linkages have *Sp* linkage phosphorus. In some embodiments, at least 10%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of all chiral internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 10%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of all internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 10%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90% or 95% of all phosphorothioate internucleotidic linkages have *Sp* linkage phosphorus. In some embodiments, the percentage is at least 20%. In some embodiments, the percentage is at least 30%. In some embodiments, the percentage

is at least 40%. In some embodiments, the percentage is at least 50%. In some embodiments, the percentage is at least 60%. In some embodiments, the percentage is at least 65%. In some embodiments, the percentage is at least 70%. In some embodiments, the percentage is at least 75%. In some embodiments, the percentage is at least 80%. In some embodiments, the percentage is at least 90%. In some embodiments, the percentage is at least 95%. In some embodiments, all chirally controlled internucleotidic linkages have *Sp* linkage phosphorus. In some embodiments, all chirally controlled phosphorothioate internucleotidic linkages have *Sp* linkage phosphorus. In some embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 5 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 6 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 7 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 8 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 9 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 10 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 11 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 12 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 13 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 14 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 15 internucleotidic linkages are chirally controlled internucleotidic linkages having *Sp* linkage phosphorus. In some embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 internucleotidic linkages are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus. In some embodiments, no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60 internucleotidic linkages are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus. In some embodiments, one and no more than one internucleotidic linkage in an oligonucleotide is a chirally controlled internucleotidic linkage having *Rp* linkage phosphorus. In some embodiments, 2 and no more than 2 internucleotidic linkages in an oligonucleotide are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus. In some embodiments, 3 and no more than 3 internucleotidic linkages in an oligonucleotide are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus. In some embodiments, 4 and no more than 4 internucleotidic linkages in an oligonucleotide are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus. In some embodiments, 5 and no more than 5 internucleotidic linkages in an oligonucleotide are chirally controlled internucleotidic linkages having *Rp* linkage phosphorus.

[00695] In some embodiments, all, essentially all or most of the internucleotidic linkages in an oligonucleotide or a portion thereof are in the *Sp* configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages in an oligonucleotide) except for one or a minority of internucleotidic linkages (e.g., 1, 2, 3, 4, or 5, and/or less than 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages in an oligonucleotide) being in the *Rp* configuration. In some embodiments, all, essentially all or most of the internucleotidic linkages in a first domain are in the *Sp* configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages, in a first domain). In some embodiments, each internucleotidic linkage in a first domain is a phosphorothioate in the *Sp* configuration. In some embodiments, each internucleotidic linkage in the a domain is a phosphorothioate in the *Sp* configuration. In some embodiments, all, essentially all or most of the internucleotidic linkages in a second domain are in the *Sp* configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages, in a second domain). In some embodiments, each internucleotidic linkage in a second domain is a phosphorothioate in the *Sp* configuration. In some embodiments, each internucleotidic linkage in a second domain is a phosphorothioate in the *Sp* configuration except for one phosphorothioate in the *Rp* configuration. In some embodiments, all, essentially all or most of the internucleotidic linkages in a subdomain of a second domain are in the *Sp* configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages, in a first subdomain of a second domain). In some embodiments, each internucleotidic linkage in a first subdomain of a second domain is a phosphorothioate in the *Sp* configuration. In some embodiments, each internucleotidic linkage in a first subdomain of second domain is a phosphorothioate in the *Sp* configuration except for one phosphorothioate in the *Rp* configuration. In some embodiments, all, essentially all or most of the internucleotidic linkages in a the second subdomain of a second domain are in the *Sp* configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages, in a second subdomain of a second

domain) except for one or a minority of internucleotidic linkages being in the *R*p configuration. In some embodiments, each internucleotidic linkage in a second subdomain of a second domain is a phosphorothioate in the *S*p configuration except for one phosphorothioate in the *R*p configuration. In some embodiments, each internucleotidic linkage in a second subdomain of a second domain is a phosphorothioate in the *S*p configuration except for one phosphorothioate in the *R*p configuration. In some embodiments, all, essentially all or most of the internucleotidic linkages in a the third subdomain of the second domain are in the *S*p configuration (e.g., about 50%-100%, 55%-100%, 60%-100%, 65%-100%, 70%-100%, 75%-100%, 80%-100%, 85%-100%, 90%-100%, 55%-95%, 60%-95%, 65%-95%, or about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 99% or more of all chirally controlled internucleotidic linkages, or of all chiral internucleotidic linkages, or of all internucleotidic linkages, in a third subdomain of a second domain. In some embodiments, each internucleotidic linkage in a third subdomain of a second domain is a phosphorothioate in the *S*p configuration except for one phosphorothioate in the *R*p configuration. In some embodiments, each internucleotidic linkage in a third subdomain of a second domain is a phosphorothioate in the *S*p configuration except for one phosphorothioate in the *R*p configuration.

[00696] In some embodiments, an oligonucleotide comprises one or more *R*p internucleotidic linkages. In some embodiments, an oligonucleotide comprises one and no more than one *R*p internucleotidic linkages. In some embodiments, an oligonucleotide comprises five or more *R*p internucleotidic linkages. In some embodiments, about 5%-50% of all chirally controlled internucleotidic linkages in an oligonucleotide are *R*p. In some embodiments, about 5%-40% of all chirally controlled internucleotidic linkages in an oligonucleotide are *R*p. In some embodiments, certain portions (e.g., domains, subdomains, etc.) may contain relatively more (in numbers and/or percentages) *R*p internucleotidic linkages, e.g., second subdomains.

[00697] In some embodiments, an oligonucleotide comprises one or more *R*p phosphorothioate internucleotidic linkages at one or more positions, e.g., -1, -2, +1, +2, +7, +8, etc. In some embodiments, an internucleotidic linkage at position -1 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -2 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +1 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +2 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, two or three internucleotidic linkages at positions -1, -2, +1, and +2 *R*p phosphorothioate internucleotidic linkages. In some embodiments, the positions are -1 and -2. In some embodiments, the positions are +1 and +2. In some embodiments, the positions are -1 and +1. In some embodiments, the positions are -1, +1 and +2. In some embodiments, the positions are -1, -2 and +1. In some embodiments, one and only one internucleotidic linkage is *R*p phosphorothioate internucleotidic linkage. In some embodiments, one and only one internucleotidic linkage is *R*p phosphorothioate internucleotidic linkage and is at position +2, +1, 1 or 2. In some embodiments, a position is +1. In some embodiments, a position is +2. In some embodiments, a position is -1. In some embodiments, a position is -2. In some embodiments, it is observed that utilization of *R*p internucleotidic linkages may improve editing efficiency by ADAR1 (p110

and/or p150) and/or ADAR2. In some embodiments, improvements of editing by ADAR1 (p110 and/or p150) are more than those by ADAR2 (no or less improvements or less editing compared to absence of *R*p).

[00698] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition wherein the composition comprises a non-random or controlled level of a plurality of oligonucleotides, wherein oligonucleotides of the plurality share a common base sequence, and share the same configuration of linkage phosphorus independently at 1-60, 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more chiral internucleotidic linkages.

[00699] In some embodiments, provided oligonucleotides comprise 2-30 chirally controlled internucleotidic linkages. In some embodiments, provided oligonucleotide compositions comprise 5-30 chirally controlled internucleotidic linkages. In some embodiments, provided oligonucleotide compositions comprise 10-30 chirally controlled internucleotidic linkages. In some embodiments, provided oligonucleotide compositions comprise 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more chirally controlled internucleotidic linkages.

[00700] In some embodiments, about 1-100% of all internucleotidic linkages are chirally controlled internucleotidic linkages. In some embodiments, about 1-100% of all chiral internucleotidic linkages are chirally controlled internucleotidic linkages. In some embodiments, a percentage is about 5%-100%. In some embodiments, a percentage is at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 965, 96%, 98%, or 99%. In some embodiments, a percentage is about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 965, 96%, 98%, or 99%.

[00701] In some embodiments, an internucleotidic linkage in the *S*p configuration (having a *S*p linkage phosphorus) is a phosphorothioate internucleotidic linkage. In some embodiments, an achiral internucleotidic linkage is a natural phosphate linkage. In some embodiments, an internucleotidic linkage in the *R*p configuration (having a *R*p linkage phosphorus) is a phosphorothioate internucleotidic linkage. In some embodiments, each internucleotidic linkage in the *S*p configuration is a phosphorothioate internucleotidic linkage. In some embodiments, each achiral internucleotidic linkage is a natural phosphate linkage. In some embodiments, each internucleotidic linkage in the *R*p configuration is a phosphorothioate internucleotidic linkage. In some embodiments, each internucleotidic linkage in the *S*p configuration is a phosphorothioate internucleotidic linkage, each achiral internucleotidic linkage is a natural phosphate linkage, and each internucleotidic linkage in the *R*p configuration is a phosphorothioate internucleotidic linkage.

[00702] In some embodiments, provided oligonucleotides in chirally controlled oligonucleotide compositions each comprise different types of internucleotidic linkages. In some embodiments, provided oligonucleotides comprise at least one natural phosphate linkage and at least one modified internucleotidic linkage. In some embodiments, provided oligonucleotides comprise at least one natural phosphate linkage and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32,

33, 34, 35, 36, 37, 38, 39 or 40 modified internucleotidic linkages. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each modified internucleotidic linkage is independently a chiral internucleotidic linkage and is independently chirally controlled.

[00703] In some embodiments, oligonucleotides in a chirally controlled oligonucleotide composition each comprise at least two internucleotidic linkages that have different stereochemistry and/or different P-modifications relative to one another. In some embodiments, at least two internucleotidic linkages have different stereochemistry relative to one another. In some embodiments, oligonucleotides each comprise a pattern of backbone chiral centers comprising alternating linkage phosphorus stereochemistry.

[00704] In some embodiments, a phosphorothioate triester linkage comprises a chiral auxiliary, which, for example, is used to control the stereoselectivity of a reaction, e.g., a coupling reaction in an oligonucleotide synthesis cycle. In some embodiments, a phosphorothioate triester linkage does not comprise a chiral auxiliary. In some embodiments, a phosphorothioate triester linkage is intentionally maintained until and/or during the administration of the oligonucleotide composition to a subject.

[00705] In some embodiments, oligonucleotides are linked to a solid support. In some embodiments, a solid support is a support for oligonucleotide synthesis. In some embodiments, a solid support comprises glass. In some embodiments, a solid support is CPG (controlled pore glass). In some embodiments, a solid support is polymer. In some embodiments, a solid support is polystyrene. In some embodiments, the solid support is Highly Crosslinked Polystyrene (HCP). In some embodiments, the solid support is hybrid support of Controlled Pore Glass (CPG) and Highly Cross-linked Polystyrene (HCP). In some embodiments, a solid support is a metal foam. In some embodiments, a solid support is a resin. In some embodiments, oligonucleotides are cleaved from a solid support.

[00706] In some embodiments, purity, particularly stereochemical purity, and particularly diastereomeric purity of many oligonucleotides and compositions thereof wherein all other chiral centers in the oligonucleotides but the chiral linkage phosphorus centers have been stereodefined (e.g., carbon chiral centers in the sugars, which are defined in, *e.g.*, phosphoramidites for oligonucleotide synthesis), can be controlled by stereoselectivity (as appreciated by those skilled in this art, diastereoselectivity in many cases of oligonucleotide synthesis wherein the oligonucleotide comprise more than one chiral centers) at chiral linkage phosphorus in coupling steps when forming chiral internucleotidic linkages. In some embodiments, a coupling step has a stereoselectivity (diastereoselectivity when there are other chiral centers) of 60% at the linkage phosphorus. After such a coupling step, the new internucleotidic linkage formed may be referred to have a 60% stereochemical purity (for oligonucleotides, typically diastereomeric purity in view of the existence of other chiral centers). In some embodiments, each coupling step independently has a stereoselectivity of at least 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%. In some embodiments, a chirally controlled internucleotidic linkage is typically formed with a stereoselectivity of at

least 85%, 87%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99.5% or virtually 100% (in some embodiments, at least 85%; in some embodiments, at least 87%; in some embodiments, at least 90%; in some embodiments, at least 95%; in some embodiments, at least 96%; in some embodiments, at least 97%; in some embodiments, at least 98%; in some embodiments, at least 99%). In some embodiments, a stereoselectivity is at least 85%. In some embodiments, a stereoselectivity is at least 87%. In some embodiments, a stereoselectivity is at least 90%. In some embodiments, each coupling step independently has a stereoselectivity of virtually 100%.

[00707] In some embodiments, stereopurity of a chiral center, e.g., a chiral linkage phosphorus, in a composition is at least 60%, 70%, 80%, 85%, 87%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 99.5%. In some embodiments, a stereopurity is at least 80%. In some embodiments, a stereopurity is at least 85%. In some embodiments, a stereopurity is at least 87%. In some embodiments, a stereopurity is at least 90%. In some embodiments, a stereopurity is virtually 100%. In some embodiments, each chirally controlled internucleotidic linkage independently has a stereochemical purity (typically diastereomeric purity for oligonucleotides with multiple chiral centers) of at least 85%, 87%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99.5% or virtually 100% (in some embodiments, at least 85%; in some embodiments, at least 87%; in some embodiments, at least 90%; in some embodiments, at least 95%; in some embodiments, at least 96%; in some embodiments, at least 97%; in some embodiments, at least 98%; in some embodiments, at least 99%) at its chiral linkage phosphorus. In some embodiments, a chirally controlled internucleotidic linkage has a stereochemical purity of at least 90%. In some embodiments, a majority of chirally controlled internucleotidic linkages independently have a stereochemical purity of at least 90%. In some embodiments, each chirally controlled internucleotidic linkage independently has a stereochemical purity of at least 90%. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all chirally controlled internucleotidic linkages are *Sp*. In some embodiments, at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all chirally controlled phosphorothioate internucleotidic linkages are *Sp*. In some embodiments, at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%, or all phosphorothioate internucleotidic linkages are chirally controlled and are *Sp*.

[00708] Stereoselectivity and stereopurity may be assessed by various technologies. In some embodiments, stereoselectivity and/or stereopurity is virtually 100% in that when a composition is analyzed by an analytical method (e.g., NMR, HPLC, etc.), virtually all detectable stereoisomers has the intended stereochemistry.

[00709] In some embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 couplings of a monomer (as appreciated by those skilled in the art in many embodiments a phosphoramidite for oligonucleotide synthesis) independently have a stereoselectivity less than about 60%, 70%, 80%, 85%, or 90% [for oligonucleotide synthesis, typically diastereoselectivity with respect to formed linkage phosphorus chiral center(s)].

[00710] In some embodiments, in stereorandom (or racemic) preparations (or stereorandom/non-chirally

controlled oligonucleotide compositions), at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 chiral internucleotidic linkages of the oligonucleotides independently have a stereochemical purity (typically diastereomeric purity for oligonucleotides comprising multiple chiral centers) less than about 60%, 65%, 70%, 75%, 80%, or 85% with respect to chiral linkage phosphorus of the internucleotidic linkage(s). In some embodiments, a stereochemistry purity (stereopurity) is less than about 60%. In some embodiments, a stereochemistry purity (stereopurity) is less than about 65%. In some embodiments, a stereochemistry purity (stereopurity) is less than about 70%. In some embodiments, a stereochemistry purity (stereopurity) is less than about 75%. In some embodiments, a stereochemistry purity (stereopurity) is less than about 80%.

[00711] In some embodiments, compounds of the present disclosure (e.g., oligonucleotides, chiral auxiliaries, etc.) comprise multiple chiral elements (e.g., multiple carbon and/or phosphorus (e.g., linkage phosphorus of chiral internucleotidic linkages) chiral centers). In some embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or more chiral elements of a provided compound (e.g., an oligonucleotide) each independently have a diastereomeric purity as described herein. In some embodiments, a diastereomeric purity is at least 85%. In some embodiments, a diastereomeric purity is at least 86%. In some embodiments, a diastereomeric purity is at least 87%. In some embodiments, a diastereomeric purity is at least 88%. In some embodiments, a diastereomeric purity is at least 89%. In some embodiments, a diastereomeric purity is at least 90%. In some embodiments, a diastereomeric purity is at least 91%. In some embodiments, a diastereomeric purity is at least 92%. In some embodiments, a diastereomeric purity is at least 93%. In some embodiments, a diastereomeric purity is at least 94%. In some embodiments, a diastereomeric purity is at least 95%. In some embodiments, a diastereomeric purity is at least 96%. In some embodiments, a diastereomeric purity is at least 97%. In some embodiments, a diastereomeric purity is at least 98%. In some embodiments, a diastereomeric purity is at least 99%.

[00712] As understood by a person having ordinary skill in the art, in some embodiments, diastereoselectivity of a coupling or diastereomeric purity of a chiral linkage phosphorus center can be assessed through the diastereoselectivity of a dimer formation or diastereomeric purity of a dimer prepared under the same or comparable conditions, wherein the dimer has the same 5'- and 3'-nucleosides and internucleotidic linkage.

[00713] Various technologies can be utilized for identifying or confirming stereochemistry of chiral elements (e.g., configuration of chiral linkage phosphorus) and/or patterns of backbone chiral centers, and/or for assessing stereoselectivity (e.g., diastereoselectivity of couple steps in oligonucleotide synthesis) and/or stereochemical purity (e.g., diastereomeric purity of internucleotidic linkages, compounds (e.g., oligonucleotides), etc.). Example technologies include NMR [e.g., 1D (one-dimensional) and/or 2D (two-dimensional) ^{1}H-^{31}P HETCOR (heteronuclear correlation spectroscopy)], HPLC, RP-HPLC, mass spectrometry, LC-MS, and cleavage of internucleotidic linkages by stereospecific nucleases, etc., which may be utilized individually or in combination. Example useful nucleases include benzonase, micrococcal nuclease,

and svPDE (snake venom phosphodiesterase), which are specific for certain internucleotidic linkages with *Rp* linkage phosphorus (e.g., a *Rp* phosphorothioate linkage); and nuclease P1, mung bean nuclease, and nuclease S1, which are specific for internucleotidic linkages with *Sp* linkage phosphorus (e.g., a *Sp* phosphorothioate linkage). Without wishing to be bound by any particular theory, the present disclosure notes that, in at least some cases, cleavage of oligonucleotides by a particular nuclease may be impacted by structural elements, e.g., chemical modifications (e.g., 2'-modifications of a sugars), base sequences, or stereochemical contexts. For example, it is observed that in some cases, benzonase and micrococcal nuclease, which are specific for internucleotidic linkages with *Rp* linkage phosphorus, were unable to cleave an isolated *Rp* phosphorothioate internucleotidic linkage flanked by *Sp* phosphorothioate internucleotidic linkages.

[00714] In some embodiments, oligonucleotides sharing a common base sequence, a common pattern of backbone linkages, and a common pattern of backbone chiral centers share a common pattern of backbone phosphorus modifications and a common pattern of base modifications. In some embodiments, oligonucleotide compositions sharing a common base sequence, a common pattern of backbone linkages, and a common pattern of backbone chiral centers share a common pattern of backbone phosphorus modifications and a common pattern of nucleoside modifications. In some embodiments, oligonucleotides share a common base sequence, a common pattern of backbone linkages, and a common pattern of backbone chiral centers have identical structures.

[00715] In some embodiments, the present disclosure provides an oligonucleotide composition comprising a plurality of oligonucleotides capable of directing deamination of a target adenosine in a target nucleic acid, wherein oligonucleotides of the plurality are of a particular oligonucleotide type, which composition is chirally controlled in that it is enriched, relative to a substantially racemic preparation of oligonucleotides having the same base sequence, for oligonucleotides of the particular oligonucleotide type.

[00716] In some embodiments, a plurality of oligonucleotides or oligonucleotides of a particular oligonucleotide type in a provided oligonucleotide composition are oligonucleotides. In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence;

a common pattern of backbone linkages; and

the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence and pattern of backbone linkages, for oligonucleotides of the plurality.

[00717] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides, wherein the oligonucleotides share:

a common base sequence;

a common pattern of backbone linkages; and

a common pattern of backbone chiral centers, which composition is a substantially pure preparation of a single oligonucleotide in that at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 93%, 95%, 96%, 97%, 98%, or 99% of the oligonucleotides in the composition have the common base sequence, the common pattern of backbone linkages, and the common pattern of backbone chiral centers.

[00718] In some embodiments, an oligonucleotide composition type is further defined by: 4) additional chemical moiety, if any.

[00719] In some embodiments, the percentage is at least about 10%. In some embodiments, the percentage is at least about 20%. In some embodiments, the percentage is at least about 30%. In some embodiments, the percentage is at least about 40%. In some embodiments, the percentage is at least about 50%. In some embodiments, the percentage is at least about 60%. In some embodiments, the percentage is at least about 70%. In some embodiments, the percentage is at least about 75%. In some embodiments, the percentage is at least about 80%. In some embodiments, the percentage is at least about 85%. In some embodiments, the percentage is at least about 90%. In some embodiments, the percentage is at least about 91%. In some embodiments, the percentage is at least about 92%. In some embodiments, the percentage is at least about 93%. In some embodiments, the percentage is at least about 94%. In some embodiments, the percentage is at least about 95%. In some embodiments, the percentage is at least about 96%. In some embodiments, the percentage is at least about 97%. In some embodiments, the percentage is at least about 98%. In some embodiments, the percentage is at least about 99%. In some embodiments, the percentage is or is greater than $(DS)^{nc}$, wherein DS and nc are each independently as described in the present disclosure.

[00720] In some embodiments, a plurality of oligonucleotides share the same constitution. In some embodiments, a plurality of oligonucleotides are identical (the same stereoisomer). In some embodiments, a chirally controlled oligonucleotide composition is a stereopure oligonucleotide composition wherein oligonucleotides of the plurality are identical (the same stereoisomer), and the composition does not contain any other stereoisomers. Those skilled in the art will appreciate that one or more other stereoisomers may exist as impurities as processes, selectivities, purifications, etc. may not achieve completeness.

[00721] In some embodiments, a provided composition is characterized in that when it is contacted with a target nucleic acid [e.g., a transcript (e.g., pre-mRNA, mature mRNA, other types of RNA, etc. that hybridizes with oligonucleotides of the composition)], levels of the target nucleic acid and/or a product encoded thereby is reduced compared to that observed under a reference condition. In some embodiments, levels of a nucleic acid and/or a product thereof, which nucleic acid is a product of an A to I edition of a target nucleic acid, is increased. In some embodiments, a reference condition is selected from the group consisting of absence of the composition, presence of a reference composition, and combinations thereof. In some embodiments, a reference condition is absence of the composition. In some embodiments, a reference condition is presence of a reference composition. In some embodiments, a reference composition is a composition whose oligonucleotides do not hybridize with the target nucleic acid. In some embodiments, a reference composition

is a composition whose oligonucleotides do not comprise a sequence that is sufficiently complementary to the target nucleic acid. In some embodiments, a reference composition is a composition whose oligonucleotides share the same base sequence but do not share the same nucleobase, sugar and/or internucleotidic linkage modifications. In some embodiments, a provided composition is a chirally controlled oligonucleotide composition and a reference composition is a non-chirally controlled oligonucleotide composition which is otherwise identical but is not chirally controlled (e.g., a racemic preparation of oligonucleotides of the same constitution as oligonucleotides of a plurality in the chirally controlled oligonucleotide composition).

[00722] In some embodiments, the present disclosure provides a chirally controlled oligonucleotide composition comprising a plurality of oligonucleotides capable of directing deamination of a target adenosine in a target nucleic acid, wherein the oligonucleotides share:

a common base sequence,

a common pattern of backbone linkages, and

the same linkage phosphorus stereochemistry at one or more chiral internucleotidic linkages (chirally controlled internucleotidic linkages),

wherein the composition is enriched, relative to a substantially racemic preparation of oligonucleotides sharing the common base sequence and pattern of backbone linkages, for oligonucleotides of the plurality,

the oligonucleotide composition being characterized in that, when it is contacted with a target sequence, deamination of the target adenosine in the target nucleic acid is improved relative to that observed under a reference condition selected from the group consisting of absence of the composition, presence of a reference composition, and combinations thereof.

[00723] As appreciated by those skilled in the art, deamination of a target adenosine can be assessed using various technologies. In some embodiments, a technology is sequencing, wherein a deaminated adenosine is detected as G or I. In some embodiments, deamination is assessed by levels of a product (e.g., RNA, protein (e.g., encoded by a sequence wherein a target A is replaced with I but is otherwise identical to a target nucleic acid), etc.).

[00724] As demonstrated herein, oligonucleotide structural elements (e.g., sugar modifications, backbone linkages, backbone chiral centers, backbone phosphorus modifications, patterns thereof, etc.) and combinations thereof can provide surprisingly improved properties and/or bioactivities.

[00725] In some embodiments, an oligonucleotide composition is a substantially pure preparation of a single oligonucleotide stereoisomer in that oligonucleotides in the composition that are of the same constitution but are not of the stereoisomer are impurities from the preparation process of said oligonucleotide stereoisomer, in some case, after certain purification procedures.

[00726] In some embodiments, the present disclosure provides oligonucleotides and oligonucleotide compositions that are chirally controlled, and in some embodiments, stereopure. For instance, in some embodiments, a provided composition contains non-random or controlled levels of one or more individual oligonucleotide types. In some embodiments, oligonucleotides of the same oligonucleotide type are identical.

Nucleobases

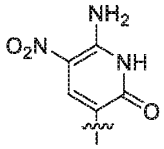
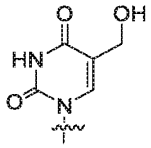
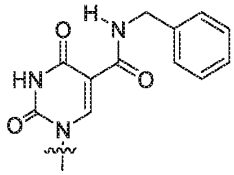
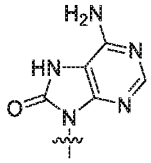
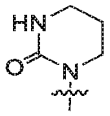
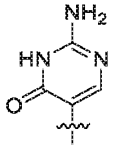
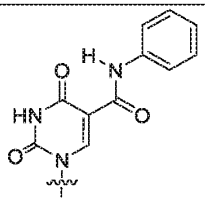
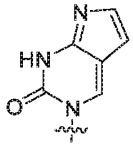
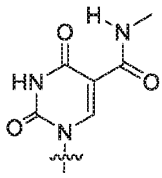
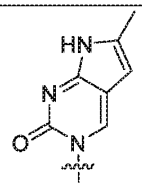
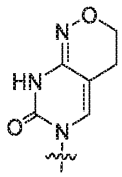
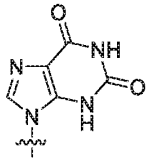
[00727] Various nucleobases may be utilized in provided oligonucleotides in accordance with the present disclosure. In some embodiments, a nucleobase is a natural nucleobase, the most commonly occurring ones being A, T, C, G and U. In some embodiments, a nucleobase is a modified nucleobase in that it is not A, T, C, G or U. In some embodiments, a nucleobase is optionally substituted A, T, C, G or U, or a substituted tautomer of A T, C, G or U. In some embodiments, a nucleobase is optionally substituted A, T, C, G or U, e.g., 5mC, 5-hydroxymethyl C, etc. In some embodiments, a nucleobase is alkyl-substituted A, T, C, G or U. In some embodiments, a nucleobase is A. In some embodiments, a nucleobase is T. In some embodiments, a nucleobase is C. In some embodiments, a nucleobase is G. In some embodiments, a nucleobase is U. In some embodiments, a nucleobase is 5mC. In some embodiments, a nucleobase is substituted A, T, C, G or U. In some embodiments, a nucleobase is a substituted tautomer of A, T, C, G or U. In some embodiments, substitution protects certain functional groups in nucleobases to minimize undesired reactions during oligonucleotide synthesis. Suitable technologies for nucleobase protection in oligonucleotide synthesis are widely known in the art and may be utilized in accordance with the present disclosure. In some embodiments, modified nucleobases improves properties and/or activities of oligonucleotides. For example, in many cases, 5mC may be utilized in place of C to modulate certain undesired biological effects, e.g., immune responses. In some embodiments, when determining sequence identity, a substituted nucleobase having the same hydrogen-bonding pattern is treated as the same as the unsubstituted nucleobase, e.g., 5mC may be treated the same as C [e.g., an oligonucleotide having 5mC in place of C (e.g., AT5mCG) is considered to have the same base sequence as an oligonucleotide having C at the corresponding location(s) (e.g., ATCG)]. In some embodiments, a nucleobase is or comprise an optionally substituted ring having at least one nitrogen atom. In some embodiments, a nucleobase comprise Ring BA as described herein, wherein at least one monocyclic ring of Ring BA comprise a nitrogen ring atom.

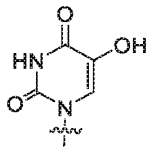
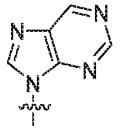
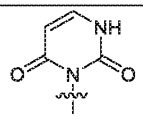
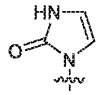
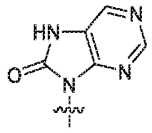
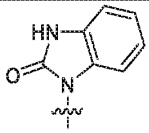
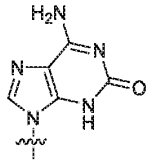
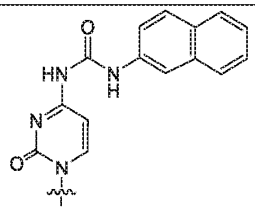
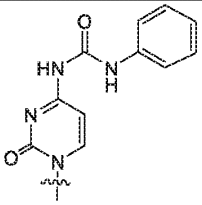
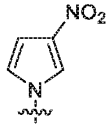
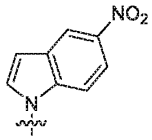
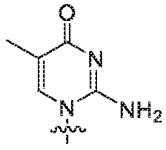
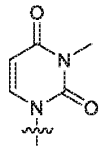
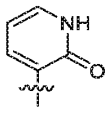
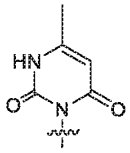
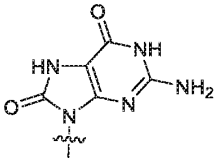
[00728] In some embodiments, an oligonucleotide comprises one or more A, T, C, G or U. In some embodiments, an oligonucleotide comprises one or more optionally substituted A, T, C, G or U. In some embodiments, an oligonucleotide comprises one or more 5-methylcytidine, 5-hydroxymethylcytidine, 5-formylcytosine, or 5-carboxylcytosine. In some embodiments, an oligonucleotide comprises one or more 5-methylcytidine. In some embodiments, each nucleobase in an oligonucleotide is selected from the group consisting of optionally substituted A, T, C, G and U, and optionally substituted tautomers of A, T, C, G and U. In some embodiments, each nucleobase in an oligonucleotide is optionally protected A, T, C, G and U. In some embodiments, each nucleobase in an oligonucleotide is optionally substituted A, T, C, G or U. In some embodiments, each nucleobase in an oligonucleotide is selected from the group consisting of A, T, C, G, U, and 5mC.

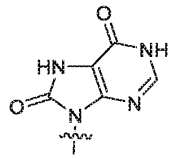
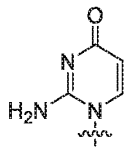
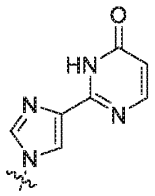
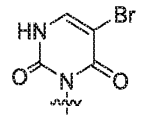
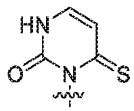
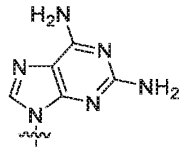
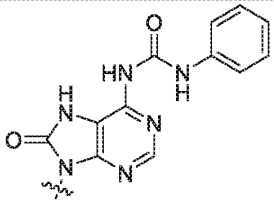
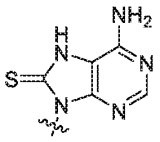
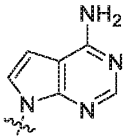
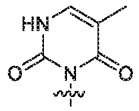
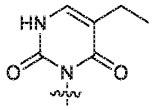
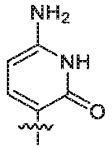
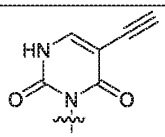
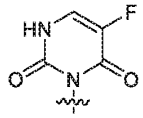
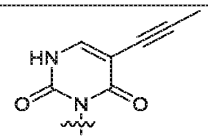
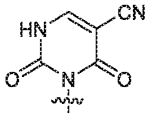
[00729] As demonstrated herein, utilization of certain nucleobases at certain locations (e.g., in a nucleoside opposite to a target adenosine and/or its adjacent nucleoside(s)) can provide oligonucleotides with improved properties and/or activities (e.g., adenosine editing to I). In some embodiments, a useful nucleobase is or

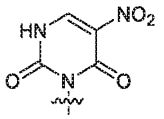
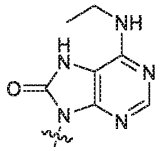
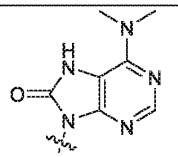
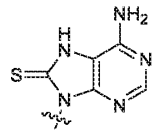
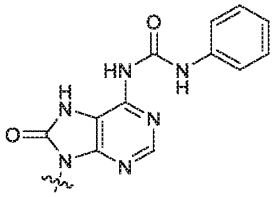
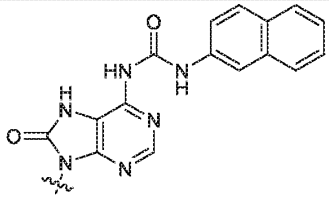
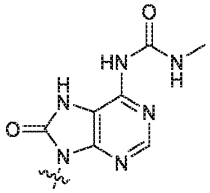
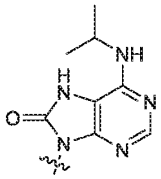
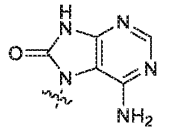
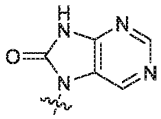
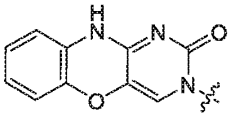
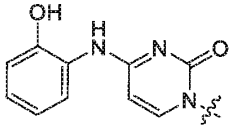
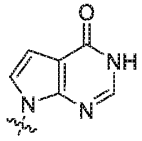
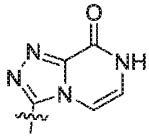
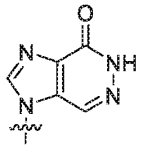
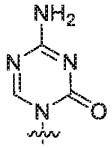
comprises Ring BA as described herein. In some embodiments, a nucleobase in a nucleoside is or comprises Ring BA which has the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA, wherein the nucleobase is optionally substituted or protected. In some embodiments, a nucleobase is optionally substituted or protected, or optionally substituted or protected tautomer of:

Table BA-1. Certain useful nucleobases.

zdnp		b007U	
b001U		b001A or [o8A]	
b002U		b001C	
b003U or [phc5U]		b002C	
b004U or [nmc5U]		b003C or [m6pyrC]	
b005U or [dhpU]		b002I or [Xan]	

b006U		b003I or [purine]	
b008U or [3nU]		b009U or [im2o]	
b002A		b003A or [o2imbc]	
b001G or [isoG]		b007C	
b004C or [pamC]		b005C or [no3pyr]	
b006C or [no5ind]		b008C or [mi5C]	
b011U or [m3U]		b012U or [o2pyr]	
b013U or [3nm6U]		b002G	

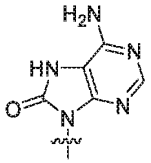
b004I or [o68pur]		b009C or [isoC]	
b014I		b014U	
b015U		b004A or [n2A]	
b005A		b006A or [s8A]	
b007A or [c7A]		[3nT]	
[3ne5U]			
		[3nfl5U]	
[3npry5U]		[3ncn5U]	

			
			
		[napth6o8A]	
		[ipr6o8A]	
			
			
[c7In]		[c39z48In]	
[z2c3In]		[z5C]	

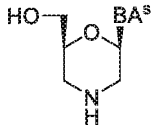
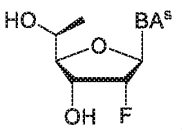
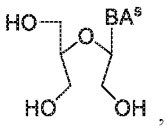
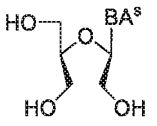
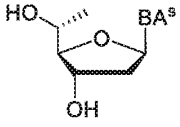
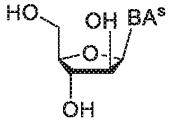
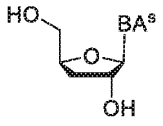
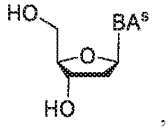
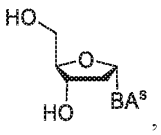
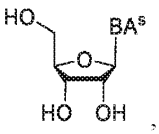
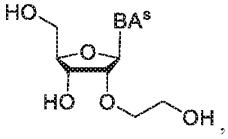
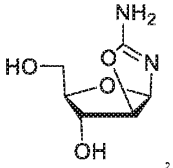
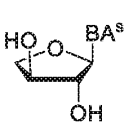
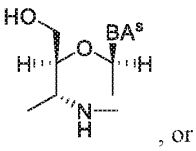
In some embodiments, a modified nucleobase is b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I,

b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [nathp6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], or zdnp. In some embodiments, the present disclosure provides oligonucleotides comprising one or more such nucleobases. In some embodiments, the present disclosure provides compounds comprising such nucleobases. In some embodiments, the present disclosure provides monomers (e.g., those useful for oligonucleotide synthesis) comprising such nucleobases. In some embodiments, the present disclosure provides phosphoramidites comprising such nucleobases. In some embodiments, phosphoramidites are CED phosphoramidites. In some embodiments, monomers comprise auxiliary moieties as described herein (e.g., with P forming bonds to O and N, to O and S, to S and S, etc.). In some embodiments, phosphoramidites comprise chiral auxiliary moieties as described herein (e.g., with P forming bonds to O and N). In some embodiments, R^{NS} comprises such a nucleobase. In some embodiments, nucleobases are protected for oligonucleotide synthesis.

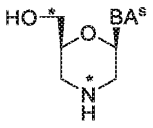
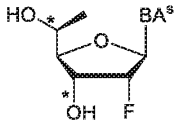
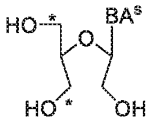
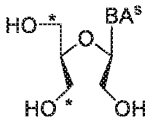
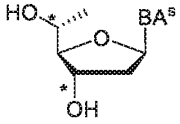
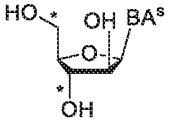
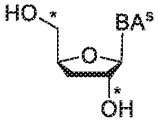
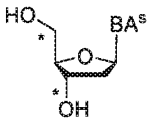
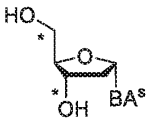
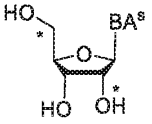
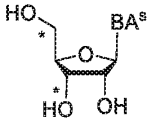
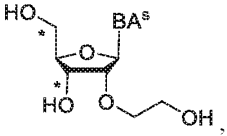
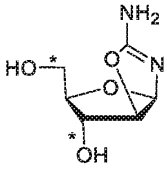
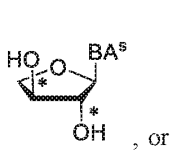
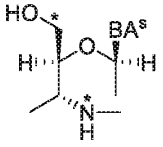
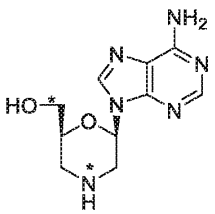
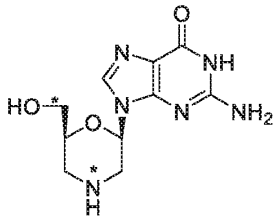
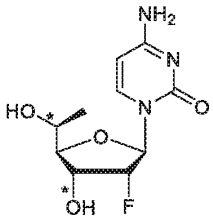
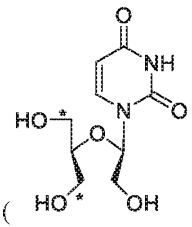
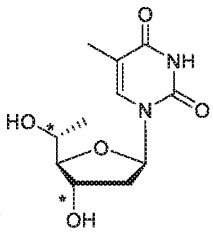
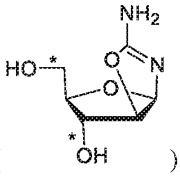
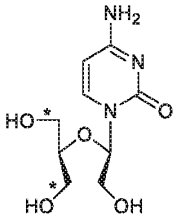
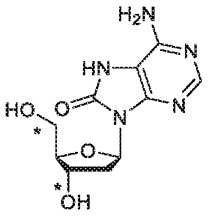
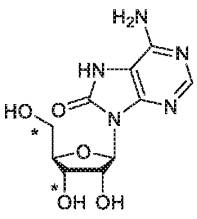
[00730] In some embodiments, the present disclosure provides various nucleosides. In some embodiments, b001U, b002U, b003U, b004U, b005U, b006U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b002A, b001G, b004C, b007U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, b009U, b003A, or b007C may also refer to a nucleoside whose nucleobase is b001U, b002U, b003U, b004U, b005U, b006U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b002A, b001G, b004C, b007U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001C, b002C, b003C, b002I, b003I, b009U, b003A, or b007C, respectively. For example, b001A may refer to a nucleoside whose nucleobase is

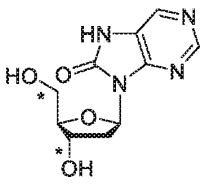


and whose sugar is a natural DNA sugar; sugar modification may also be indicated, for example, "r" in b001rA indicates there is a 2'-OH on the sugar (a natural RNA sugar). In some embodiments, the present disclosure provides a compound having the structure of

a salt thereof, wherein BA^s is as described herein. In some embodiments, a provided compound, e.g., a

nucleoside has the structure of , , , , , , , , , , , , , , or , or a salt thereof, wherein "*" indicates connection to internucleotidic linkages when in various oligonucleotides, and BA^s is as described herein. In some embodiments, BA^s is a nucleobase, e.g., BA as described herein. In some embodiments, BA is protected for oligonucleotide synthesis. In some embodiments, a provided nucleoside is selected from Asm01 (), Gsm01 (), 5MSfC (), Usm04 (), 5MRdT (),L034 (), Csm04 (), b001A (), b001rA (), b002A (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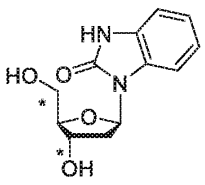
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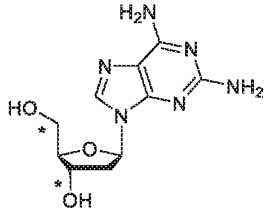
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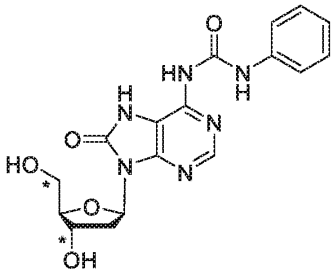
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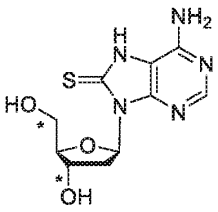
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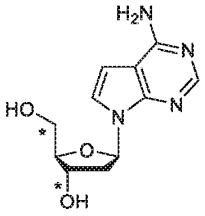
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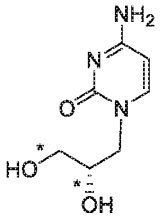
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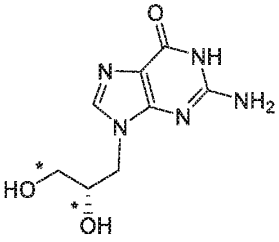
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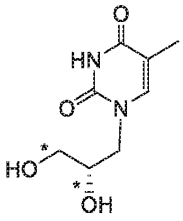
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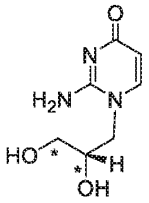
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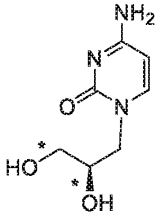
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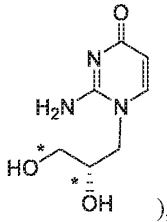
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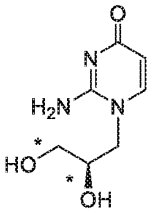
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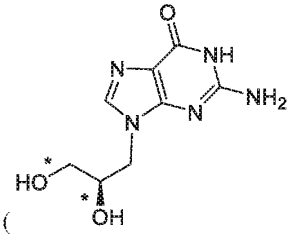
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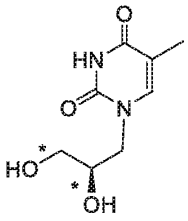
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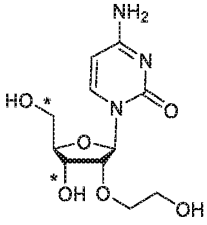
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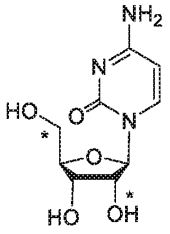
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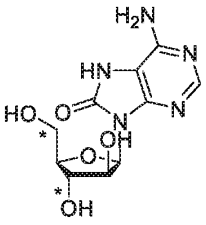
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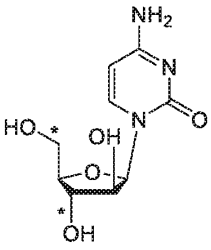
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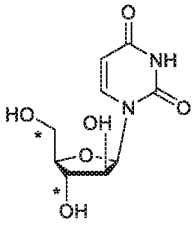
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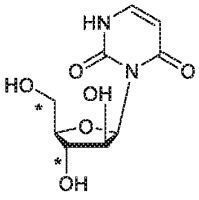
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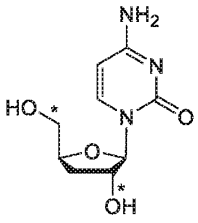
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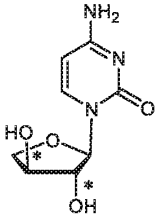
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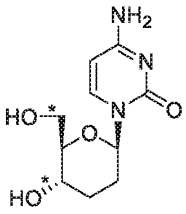
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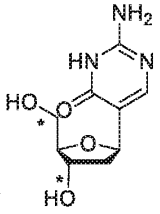
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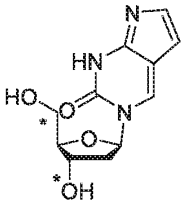
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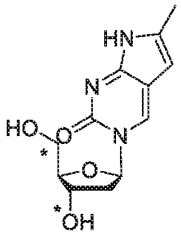
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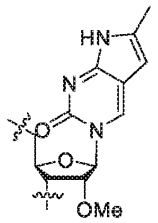
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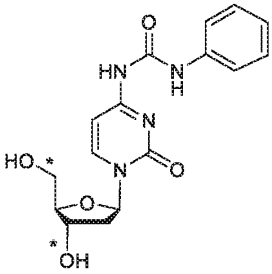
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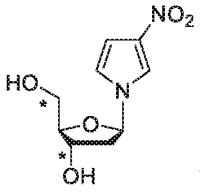
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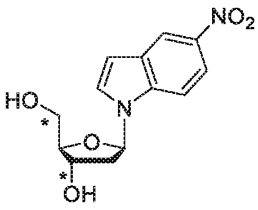
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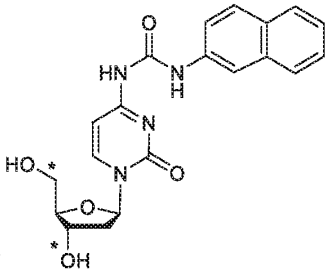
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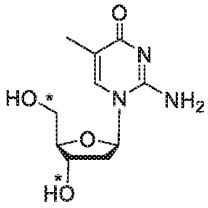
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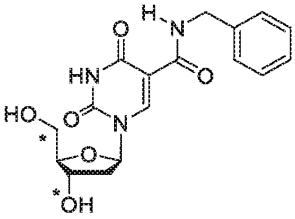
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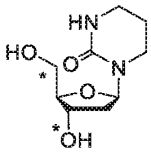
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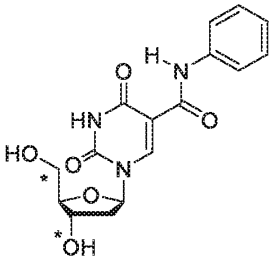
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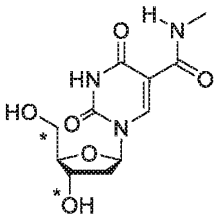
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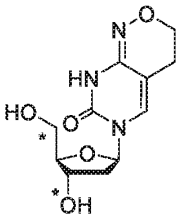
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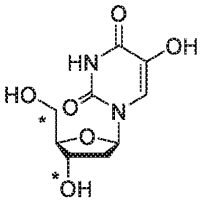
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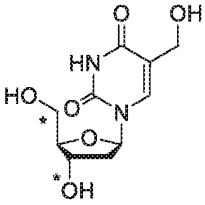
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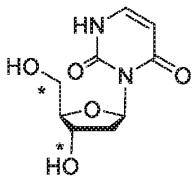
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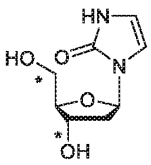
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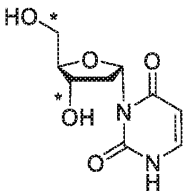
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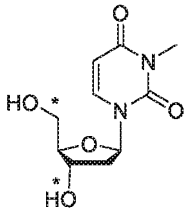
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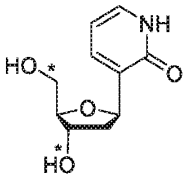
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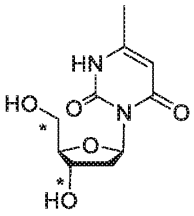
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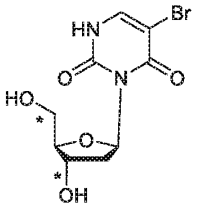
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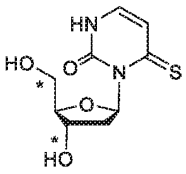
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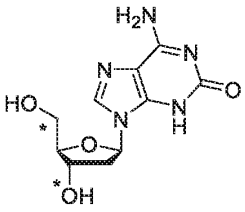
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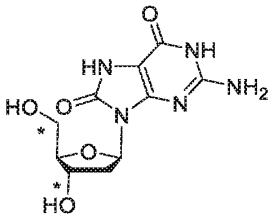
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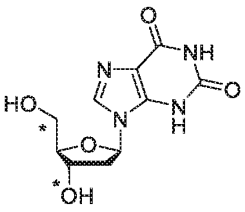
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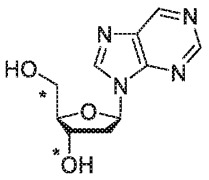
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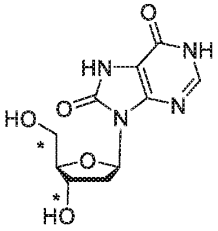
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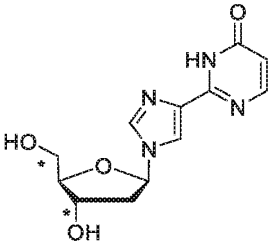
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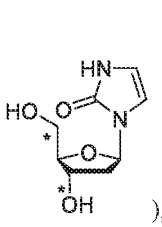
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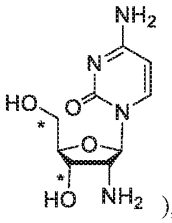
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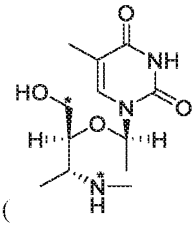
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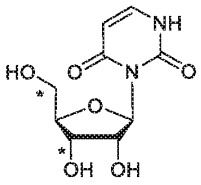
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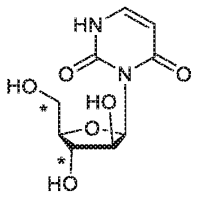
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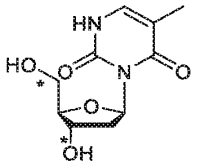
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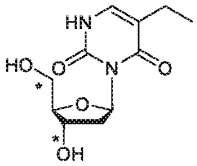
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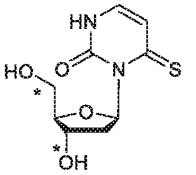
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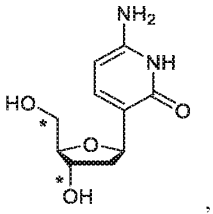
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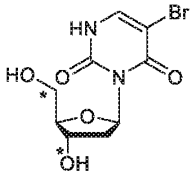
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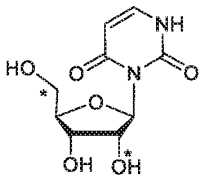
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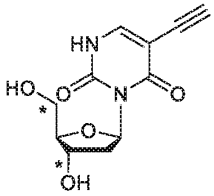
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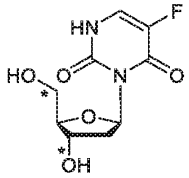
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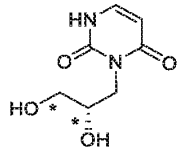
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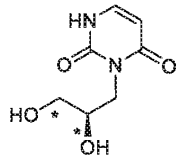
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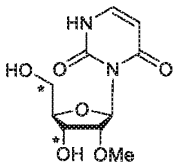
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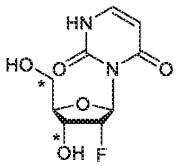
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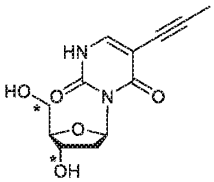
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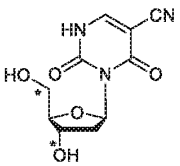
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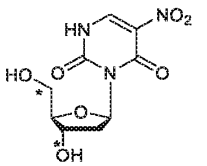
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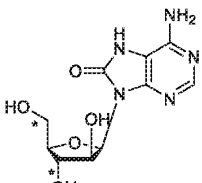
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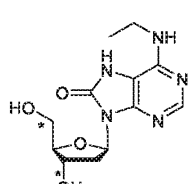
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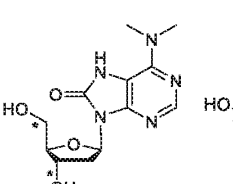
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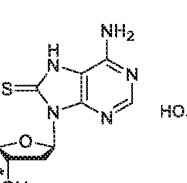
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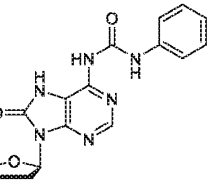
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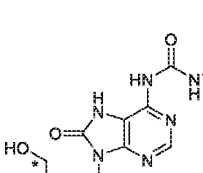
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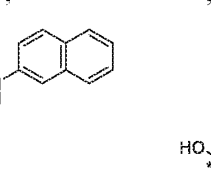
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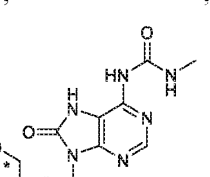
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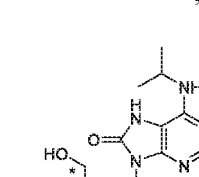
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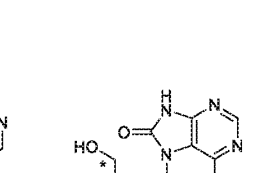
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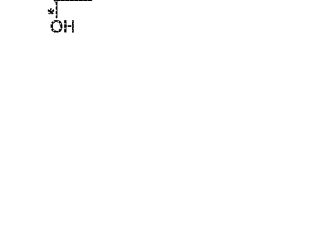
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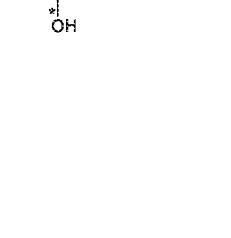
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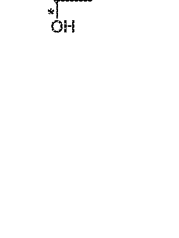
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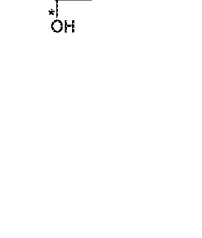
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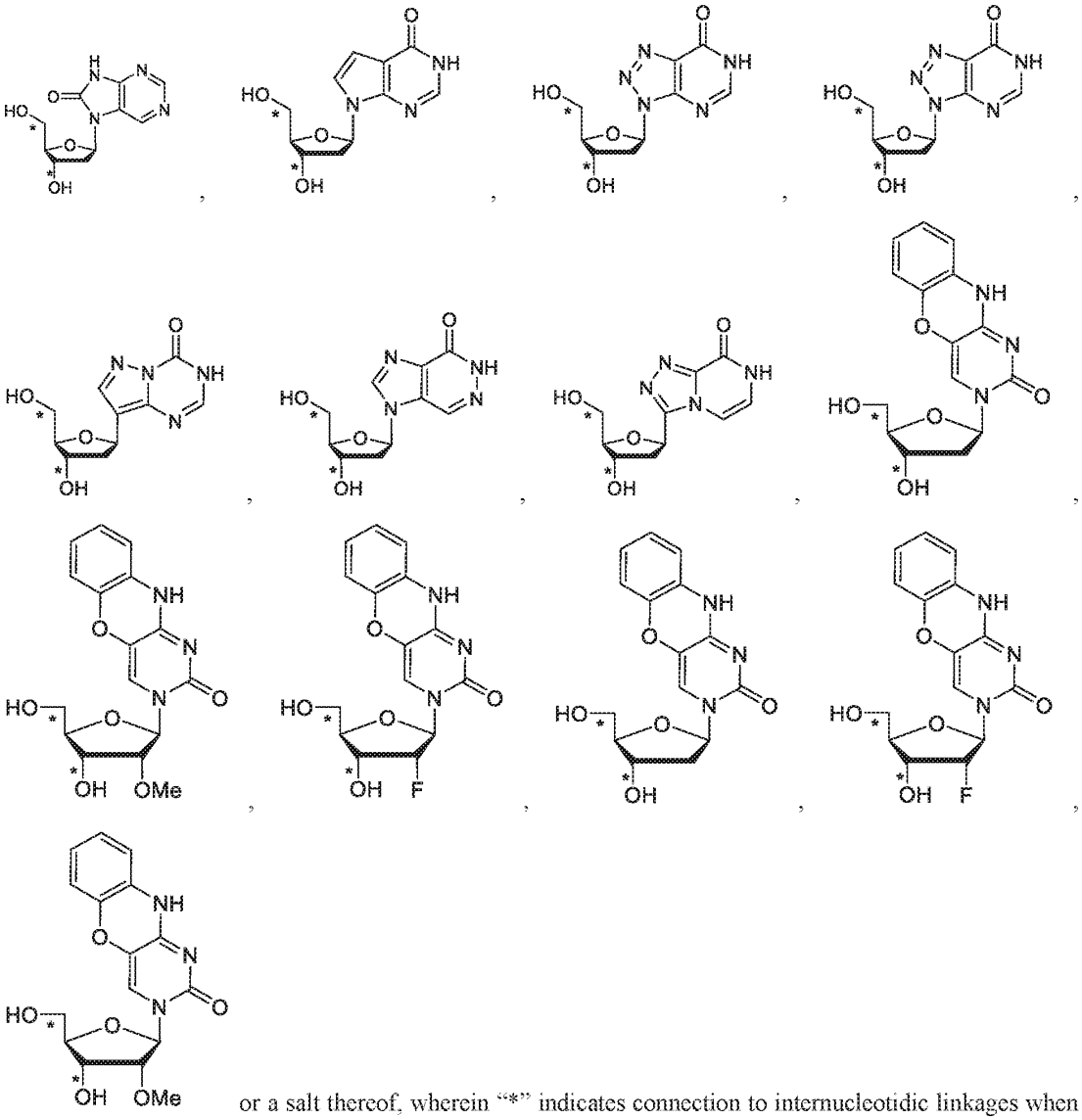
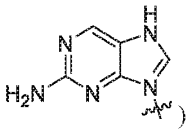
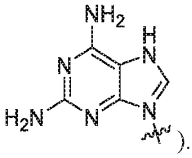


or a salt thereof, wherein "*" indicates connection to internucleotidic linkages when in various oligonucleotides. In some embodiments, an oligonucleotide comprises a nucleoside described herein. In some embodiments, a nucleoside is connected to a internucleotidic linkage through a nitrogen atom (e.g., sm01, sm18, etc.), wherein the nitrogen atom is directly connected to a linkage phosphorus atom. In some embodiments, the present disclosure provides monomers of nucleosides (e.g., Asm01, Gsm01, Tsm18, etc.) as described herein. In some embodiments, the present disclosure provides phosphoramidites of nucleosides as described herein. In some embodiments, such monomers or phosphoramidites comprise protected hydroxyl (e.g., DMTrO−) and/or protected nucleobases (e.g., for oligonucleotide synthesis). In some embodiments, such monomers or phosphoramidites comprise protected hydroxyl (e.g., DMTrO−), optionally protected nucleobases (e.g., as useful for oligonucleotide synthesis), and/or chiral auxiliary groups. Certain

reagents, such as various phosphoramidites, that are useful for incorporating various nucleosides and/or compounds into oligonucleotides, and certain technologies for utilizing such reagents for oligonucleotide preparation, e.g., cycles, conditions, etc., are described in the Examples, WO 2021/071858, or WO 2022/099159. Certain oligonucleotides comprising modified nucleosides and compositions thereof are prepared utilizing such reagents and technologies and are presented herein as examples, e.g., those in various Tables including those in Table 1 and Table 1A.

[00731] In some embodiments, the present disclosure provides oligonucleotides comprising one or more modified nucleobases as described herein. In some embodiments, the present disclosure provides compounds comprising modified nucleobases as described herein. In some embodiments, the present disclosure provides monomers (e.g., those useful for oligonucleotide synthesis) comprising modified nucleobases as described herein. In some embodiments, the present disclosure provides phosphoramidites comprising modified nucleobases as described herein. In some embodiments, phosphoramidites are CED phosphoramidites. In some embodiments, monomers comprise auxiliary moieties as described herein (e.g., with P forming bonds to O and N, to O and S, to S and S, etc.). In some embodiments, phosphoramidites comprise chiral auxiliary moieties as described herein (e.g., with P forming bonds to O and N). In some embodiments, R^{NS} comprises a nucleobase as described herein. In some embodiments, R^{NS} comprises a modified nucleobase as described herein. In some embodiments, nucleobases are protected for oligonucleotide synthesis.

[00732] In some embodiments, an oligonucleotide comprises one or more structures independently selected from pseudoisocytidine, Benner's base Z, 5-hydroxyC, 5-aminoC and 8-oxoA.

[00733] In some embodiments, a nucleobase is optionally substituted 2AP (2-amino purine, ) or DAP (2,6-diamino purine, ). In some embodiments, a nucleobase is optionally substituted 2AP. In some embodiments, a nucleobase is optionally substituted DAP. In some embodiments, a nucleobase is 2AP. In some embodiments, a nucleobase is DAP.

[00734] As appreciated by those skilled in the art, various nucleobases are known in the art and can be utilized in accordance with the present disclosure, e.g., those described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the sugar, base, and internucleotidic linkage modifications of each of which are independently incorporated herein by reference. In some embodiments, nucleobases are protected and useful for oligonucleotide synthesis.

[00735] In some embodiments, a nucleobase is a natural nucleobase or a modified nucleobase derived from

a natural nucleobase. Examples include uracil, thymine, adenine, cytosine, and guanine optionally having their respective amino groups protected by acyl protecting groups, 2-fluorouracil, 2-fluorocytosine, 5-bromouracil, 5-iodouracil, 2,6-diaminopurine, azacytosine, pyrimidine analogs such as pseudoisocytosine and pseudouracil and other modified nucleobases such as 8-substituted purines, xanthine, or hypoxanthine (the latter two being the natural degradation products). Certain examples of modified nucleobases are disclosed in Chiu and Rana, RNA, 2003, 9, 1034-1048, Limbach et al. Nucleic Acids Research, 1994, 22, 2183-2196 and Revankar and Rao, Comprehensive Natural Products Chemistry, vol. 7, 313. In some embodiments, a modified nucleobase is substituted uracil, thymine, adenine, cytosine, or guanine. In some embodiments, a modified nucleobase is a functional replacement, e.g., in terms of hydrogen bonding and/or base pairing, of uracil, thymine, adenine, cytosine, or guanine. In some embodiments, a nucleobase is optionally substituted uracil, thymine, adenine, cytosine, 5-methylcytosine, or guanine. In some embodiments, a nucleobase is uracil, thymine, adenine, cytosine, 5-methylcytosine, or guanine.

[00736] In some embodiments, a provided oligonucleotide comprises one or more 5-methylcytosine. In some embodiments, the present disclosure provides an oligonucleotide whose base sequence is disclosed herein, e.g., in Table 1 or Table 1A, wherein each T may be independently replaced with U and vice versa, and each cytosine is optionally and independently replaced with 5-methylcytosine or vice versa. As appreciated by those skilled in the art, in some embodiments, 5mC may be treated as C with respect to base sequence of an oligonucleotide - such oligonucleotide comprises a nucleobase modification at the C position (e.g., see various oligonucleotides in Table 1 or Table 1A). In description of oligonucleotides, typically unless otherwise noted, nucleobases, sugars and internucleotidic linkages are non-modified.

[00737] In some embodiments, a modified base is optionally substituted adenine, cytosine, guanine, thymine, or uracil, or a tautomer thereof. In some embodiments, a modified nucleobase is a modified adenine, cytosine, guanine, thymine or uracil, modified by one or more modifications by which:

a nucleobase is modified by one or more optionally substituted groups independently selected from acyl, halogen, amino, azide, alkyl, alkenyl, alkynyl, aryl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, heteroaryl, carboxyl, hydroxyl, biotin, avidin, streptavidin, substituted silyl, and combinations thereof;

one or more atoms of a nucleobase are independently replaced with a different atom selected from carbon, nitrogen and sulfur;

one or more double bonds in a nucleobase are independently hydrogenated; or

one or more aryl or heteroaryl rings are independently inserted into a nucleobase.

[00738] In some embodiments, a base is optionally substituted A, T, C, G or U, wherein one or more $-NH_2$ are independently and optionally replaced with $-C(-L-R^1)_3$, one or more $-NH-$ are independently and optionally replaced with $-C(-L-R^1)_2-$, one or more $=N-$ are independently and optionally replaced with $-C(-L-R^1)-$, one or more $=CH-$ are independently and optionally replaced with $=N-$, and one or more $=O$ are independently and optionally replaced with $=S$, $=N(-L-R^1)$, or $=C(-L-R^1)_2$, wherein two or more $-L-R^1$

are optionally taken together with their intervening atoms to form a 3-30 membered bicyclic or polycyclic ring having 0-10 heteroatom ring atoms. In some embodiments, a modified base is optionally substituted A, T, C, G or U, wherein one or more $-NH_2$ are independently and optionally replaced with $-C(-L-R^1)_3$, one or more $-NH-$ are independently and optionally replaced with $-C(-L-R^1)_2-$, one or more $=N-$ are independently and optionally replaced with $-C(-L-R^1)-$, one or more $=CH-$ are independently and optionally replaced with $=N-$, and one or more $=O$ are independently and optionally replaced with $=S$, $=N(-L-R^1)$, or $=C(-L-R^1)_2$, wherein two or more $-L-R^1$ are optionally taken together with their intervening atoms to form a 3-30 membered bicyclic or polycyclic ring having 0-10 heteroatom ring atoms, wherein the modified base is different than the natural A, T, C, G and U. In some embodiments, a base is optionally substituted A, T, C, G or U. In some embodiments, a modified base is substituted A, T, C, G or U, wherein the modified base is different than the natural A, T, C, G and U.

[00739] In some embodiments, a modified nucleobase is a modified nucleobase known in the art, e.g., WO2017/210647. In some embodiments, modified nucleobases are expanded-size nucleobases in which one or more aryl and/or heteroaryl rings, such as phenyl rings, have been added. Certain examples of modified nucleobases, including nucleobase replacements, are described in the Glen Research catalog (Glen Research, Sterling, Virginia); Krueger AT et al., Acc. Chem. Res., 2007, 40, 141-150; Kool, ET, Acc. Chem. Res., 2002, 35, 936-943; Benner S.A., et al., Nat. Rev. Genet., 2005, 6, 553-543; Romesberg, F.E., et al., Curr. Opin. Chem. Biol., 2003, 7, 723-733; or Hirao, I., Curr. Opin. Chem. Biol., 2006, 10, 622-627. In some embodiments, an expanded-size nucleobase is an expanded-size nucleobase described in, e.g., WO2017/210647. In some embodiments, modified nucleobases are moieties such as corrin- or porphyrin-derived rings. Certain porphyrin-derived base replacements have been described in, e.g., Morales-Rojas, H and Kool, ET, Org. Lett., 2002, 4, 4377-4380. In some embodiments, a porphyrin-derived ring is a porphyrin-derived ring described in, e.g., WO2017/219647. In some embodiments, a modified nucleobase is a modified nucleobase described in, e.g., WO2017/219647. In some embodiments, a modified nucleobase is fluorescent. Examples of such fluorescent modified nucleobases include phenanthrene, pyrene, stillbene, isoxanthine, isozanthopterin, terphenyl, terthiophene, benzoterthiophene, coumarin, lumazine, tethered stillbene, benzo-uracil, naphtho-uracil, etc., and those described in e.g., WO2017/210647. In some embodiments, a nucleobase or modified nucleobase is selected from: C5-propyne T, C5-propyne C, C5-Thiazole, phenoxazine, 2-thio-thymine, 5-triazolylphenyl-thymine, diaminopurine, and N2-aminopropylguanine.

[00740] In some embodiments, a modified nucleobase is selected from 5-substituted pyrimidines, 6-azapyrimidines, alkyl or alkynyl substituted pyrimidines, alkyl substituted purines, and N-2, N-6 and O-6 substituted purines. In certain embodiments, modified nucleobases are selected from 2-aminopropyladenine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-N-methylguanine, 6-N-methyladenine, 2-propyladenine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-propynyl ($-C\equiv C-CH_3$) uracil, 5-propynylcytosine, 6-azouracil, 6-azocytosine, 6-azothymine, 5-ribosyluracil (pseudouracil), 4-

thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl, 8-aza and other 8-substituted purines, 5-halo, particularly 5-bromo, 5-trifluoromethyl, 5-halouracil, and 5-halocytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-aminoadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 6-N-benzoyladenine, 2-N-isobutyrylguanine, 4-N-benzoylcytosine, 4-N-benzoyluracil, 5-methyl 4-N-benzoylcytosine, 5-methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. In some embodiments, modified nucleobases are tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one or 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2- one (G-clamp). In some embodiments, modified nucleobases are those in which the purine or pyrimidine base is replaced with other heterocycles, for example, 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine or 2- pyridone. In some embodiments, modified nucleobases are those disclosed in US 3687808, The Concise Encyclopedia Of Polymer Science And Engineering, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990, 858-859; Englisch et al., Angewandte Chemie, International Edition, 1991, 30, 613; Sanghvi, Y.S., Chapter 15, Antisense Research and Applications, Crooke, S.T. and Lebleu, B., Eds., CRC Press, 1993, 273-288; or in Chapters 6 and 15, Antisense Drug Technology, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

[00741] In some embodiments, modified nucleobases and methods thereof are those described in US 20030158403, US 3687808, US 4845205, US 5130302, US 5134066, US 5 175273, US 5367066, US 5432272, US 5434257, US 5457187, US 5459255, US 5484908, US 5502177, US 5525711, US 5552540, US 5587469, US 5594 121, US 5596091, US 5614617, US 5645985, US 5681941, US 5750692, US 5763588, US 5830653, or US 6005096.

[00742] In some embodiments, a modified nucleobase is substituted. In some embodiments, a modified nucleobase is substituted such that it contains, e.g., heteroatoms, alkyl groups, or linking moieties connected to fluorescent moieties, biotin or avidin moieties, or other protein or peptides. In some embodiments, a modified nucleobase is a "universal base" that is not a nucleobase in the most classical sense, but that functions similarly to a nucleobase. One example of a universal base is 3-nitropyrrole.

[00743] In some embodiments, nucleosides that can be utilized in provided technologies comprise modified nucleobases and/or modified sugars, e.g., 4-acetylcytidine; 5-(carboxyhydroxylmethyl)uridine; 2'-O-methylcytidine; 5-carboxymethylaminomethyl-2-thiouridine; 5-carboxymethylaminomethyluridine; dihydrouridine; 2'-O-methylpseudouridine; beta,D-galactosylqueosine; 2'-O-methylguanosine; N^6-isopentenyladenosine; 1-methyladenosine; 1-methylpseudouridine; 1-methylguanosine; 1-methylinosine; 2,2-dimethylguanosine; 2-methyladenosine; 2-methylguanosine; N^7-methylguanosine; 3-methyl-cytidine; 5-methylcytidine; 5-hydroxymethylcytidine; 5-formylcytosine; 5-carboxylcytosine; N^6-methyladenosine; 7-methylguanosine; 5-methylaminoethyluridine; 5-methoxyaminomethyl-2-thiouridine; beta,D-mannosylqueosine; 5-methoxycarbonylmethyluridine; 5-methoxyuridine; 2-methylthio-N^6-isopentenyladenosine; N-((9-beta,D-ribofuranosyl-2-methylthiopurine-6-yl)carbamoyl)threonine; N-((9-beta,D-ribofuranosylpurine-6-yl)-N-methylcarbamoyl)threonine; uridine-5-oxyacetic acid methylester;

uridine-5-oxyacetic acid (v); pseudouridine; queosine; 2-thiocytidine; 5-methyl-2-thiouridine; 2-thiouridine; 4-thiouridine; 5-methyluridine; 2'-O-methyl-5-methyluridine; and 2'-O-methyluridine.

[00744] In some embodiments, a nucleobase, e.g., a modified nucleobase comprises one or more biomolecule binding moieties such as e.g., antibodies, antibody fragments, biotin, avidin, streptavidin, receptor ligands, or chelating moieties. In other embodiments, a nucleobase is 5-bromouracil, 5-iodouracil, or 2,6-diaminopurine. In some embodiments, a nucleobase comprises substitution with a fluorescent or biomolecule binding moiety. In some embodiments, a substituent is a fluorescent moiety. In some embodiments, a substituent is biotin or avidin.

[00745] Certain examples of nucleobases and related methods are described in US 3687808, 4845205, US 513030, US 5134066, US 5175273, US 5367066, US 5432272, US 5457187, US 5457191, US 5459255, US 5484908, US 5502177, US 5525711, US 5552540, US 5587469, US 5594121, US 5596091, US 5614617, US 5681941, US 5750692, US 6015886, US 6147200, US 6166197, US 6222025, US 6235887, US 6380368, US 6528640, US 6639062, US 6617438, US 7045610, US 7427672, US or US 7495088.

[00746] In some embodiments, an oligonucleotide comprises a nucleobase, sugar, nucleoside, and/or internucleotidic linkage which is described in any of: Gryaznov, S; Chen, J.-K. J. Am. Chem. Soc. 1994, 116, 3143; Hendrix et al. 1997 Chem. Eur. J. 3: 110; Hyrup et al. 1996 Bioorg. Med. Chem. 4: 5; Jepsen et al. 2004 Oligo. 14: 130-146; Jones et al. J. Org. Chem. 1993, 58, 2983; Koizumi et al. 2003 Nuc. Acids Res. 12: 3267-3273; Koshkin et al. 1998 Tetrahedron 54: 3607-3630; Kumar et al. 1998 Bioo. Med. Chem. Let. 8: 2219-2222; Lauritsen et al. 2002 Chem. Comm. 5: 530-531; Lauritsen et al. 2003 Bioo. Med. Chem. Lett. 13: 253-256; Mesmaeker et al. Angew. Chem., Int. Ed. Engl. 1994, 33, 226; Morita et al. 2001 Nucl. Acids Res. Supp. 1: 241-242; Morita et al. 2002 Bioo. Med. Chem. Lett. 12: 73-76; Morita et al. 2003 Bioo. Med. Chem. Lett. 2211-2226; Nielsen et al. 1997 Chem. Soc. Rev. 73; Nielsen et al. 1997 J. Chem. Soc. Perkins Transl. 1: 3423-3433; Obika et al. 1997 Tetrahedron Lett. 38 (50): 8735–8; Obika et al. 1998 Tetrahedron Lett. 39: 5401-5404; Pallan et al. 2012 Chem. Comm. 48: 8195-8197; Petersen et al. 2003 TRENDS Biotech. 21: 74-81; Rajwanshi et al. 1999 Chem. Commun. 1395-1396; Schultz et al. 1996 Nucleic Acids Res. 24: 2966; Seth et al. 2009 J. Med. Chem. 52: 10-13; Seth et al. 2010 J. Med. Chem. 53: 8309-8318; Seth et al. 2010 J. Org. Chem. 75: 1569-1581; Seth et al. 2012 Bioo. Med. Chem. Lett. 22: 296-299; Seth et al. 2012 Mol. Ther-Nuc. Acids. 1, e47; Seth, Punit P; Siwkowski, Andrew; Allerson, Charles R; Vasquez, Guillermo; Lee, Sam; Prakash, Thazha P; Kinberger, Garth; Migawa, Michael T; Gaus, Hans; Bhat, Balkrishen; et al. From Nucleic Acids Symposium Series (2008), 52(1), 553-554; Singh et al. 1998 Chem. Comm. 1247-1248; Singh et al. 1998 J. Org. Chem. 63: 10035-39; Singh et al. 1998 J. Org. Chem. 63: 6078-6079; Sorensen 2003 Chem. Comm. 2130-2131; Ts'o et al. Ann. N. Y. Acad. Sci. 1988, 507, 220; Van Aerschot et al. 1995 Angew. Chem. Int. Ed. Engl. 34: 1338; Vasseur et al. J. Am. Chem. Soc. 1992, 114, 4006; WO 2007090071; or WO 2016/079181.

[00747] In some embodiments, an oligonucleotide comprises a modified nucleobase, nucleoside or nucleotide which is described in any of: Feldman et al. 2017 J. Am. Chem. Soc. 139: 11427-11433, Feldman et al. 2017 Proc. Natl. Acad. Sci. USA 114: E6478-E6479, Hwang et al. 2009 Nucl. Acids Res. 37: 4757-4763,

Hwang et al. 2008 J. Am. Chem. Soc. 130: 14872-14882, Lavergne et al. 2012 Chem. Eur. J. 18: 1231-1239, Lavergne et al. 2013 J. Am. Chem. Soc. 135: 5408-5419, Ledbetter et al. 2018 J. Am. Chem. Soc. 140: 758-765, Malyshev et al. 2009 J. Am. Chem. Soc. 131: 14620-14621, Seo et al. 2009 Chem. Bio. Chem. 10: 2394-2400, e.g., d3FB, d2Py analogs, d2Py, d3MPy, d4MPy, d5MPy, d34DMPy, d35DMPy, d45DMPy, d5FM, d5PrM, d5SICS, dFEMO, dMMO2, dNaM, dNM01, dTPT3, nucleotides with 2'-azido, 2'-chloro, 2'-amino or arabinose sugars, isocarbostiryl-, napthyl- and azaindole-nucleotides, and modifications and derivatives and functionalized versions thereof, e.g., those in which the sugar comprises a 2'-modification and/or other modification, and dMMO2 derivatives with meta-chlorine, -bromine, -iodine, -methyl, or -propinyl substituents.

[00748] In some embodiments, a nucleobase comprises at least one optionally substituted ring which comprises a heteroatom ring atom. In some embodiments, a nucleobase comprises at least one optionally substituted ring which comprises a nitrogen ring atom. In some embodiments, such a ring is aromatic. In some embodiments, a nucleobase is bonded to a sugar through a heteroatom. In some embodiments, a nucleobase is bonded to a sugar through a nitrogen atom. In some embodiments, a nucleobase is bonded to a sugar through a ring nitrogen atom.

[00749] In some embodiments, an oligonucleotide comprises a nucleobase or modified nucleobase as described in: WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the bases and modified nucleobases of each of which are independently incorporated herein by reference.

[00750] In some embodiments, a nucleobase is an optionally substituted purine base residue. In some embodiments, a nucleobase is a protected purine base residue. In some embodiments, a nucleobase is an optionally substituted adenine residue. In some embodiments, a nucleobase is a protected adenine residue. In some embodiments, a nucleobase is an optionally substituted guanine residue. In some embodiments, a nucleobase is a protected guanine residue. In some embodiments, a nucleobase is an optionally substituted cytosine residue. In some embodiments, a nucleobase is a protected cytosine residue. In some embodiments, a nucleobase is an optionally substituted thymine residue. In some embodiments, a nucleobase is a protected thymine residue. In some embodiments, a nucleobase is an optionally substituted uracil residue. In some embodiments, a nucleobase is a protected uracil residue. In some embodiments, a nucleobase is an optionally substituted 5-methylcytosine residue. In some embodiments, a nucleobase is a protected 5-methylcytosine residue.

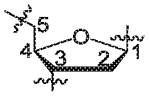
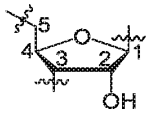
[00751] In some embodiments, a provided oligonucleotide comprises a modified nucleobase described in, e.g., US 5552540, US 6222025, US 6528640, US 4845205, US 5681941, US 5750692, US 6015886, US 5614617, US 6147200, US 5457187, US 6639062, US 7427672, US 5459255, US 5484908, US 7045610, US 3687808, US 5502177, US 5525711 6235887, US 5175273, US 6617438, US 5594121, US 6380368, US 5367066, US 5587469, US 6166197, US 5432272, US 7495088, US 5134066, or US 5596091. In some

embodiments, a nucleobase is described in WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, or WO 2020/252376, and can be utilized in accordance with the present disclosure.

[00752] In some embodiments, a nucleobase is a protected base residue as used in oligonucleotide preparation. In some embodiments, a nucleobase is a base residue illustrated in US 2011/0294124, US 2015/0211006, US 2015/0197540, WO 2015/107425, WO 2017/192679, WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the base residues of each of which are independently incorporated herein by reference.

Sugars

[00753] Various sugars, including modified sugars, can be utilized in accordance with the present disclosure. In some embodiments, the present disclosure provides sugar modifications and patterns thereof optionally in combination with other structural elements (e.g., internucleotidic linkage modifications and patterns thereof, pattern of backbone chiral centers thereof, etc.) that when incorporated into oligonucleotides can provide improved properties and/or activities.

[00754] The most common naturally occurring nucleosides comprise ribose sugars (e.g., in RNA) or deoxyribose sugars (e.g., in DNA) linked to the nucleobases adenosine (A), cytosine (C), guanine (G), thymine (T) or uracil (U). In some embodiments, a sugar, e.g., various sugars in many oligonucleotides in Table 1 or Table 1A (unless otherwise noted), is a natural DNA sugar (in DNA nucleic acids or oligonucleotides, having the structure of , wherein a nucleobase is attached to the 1' position, and the 3' and 5' positions are connected to internucleotidic linkages (as appreciated by those skilled in the art, if at the 5'-end of oligonucleotide, the 5' position may be connected to a 5'-end group (e.g., −OH)), and if at the 3'-end of an oligonucleotide, the 3' position may be connected to a 3'-end group (e.g., −OH)). In some embodiments, a sugar is a natural RNA sugar (in RNA nucleic acids or oligonucleotides, having the structure of , wherein a nucleobase is attached to the 1' position, and the 3' and 5' positions are connected to internucleotidic linkages (as appreciated by those skilled in the art, if at the 5'-end of an oligonucleotide, the 5' position may be connected to a 5'-end group (e.g., −OH), and if at the 3'-end of an oligonucleotide, the 3' position may be connected to a 3'-end group (e.g., −OH)). In some embodiments, a sugar is a modified sugar in that it is not a natural DNA sugar or a natural RNA sugar. Among other things, modified sugars may provide improved stability. In some embodiments, modified sugars can be utilized to alter and/or optimize one or more hybridization characteristics. In some embodiments, modified sugars can be utilized to alter and/or optimize

target nucleic acid recognition. In some embodiments, modified sugars can be utilized to optimize Tm. In some embodiments, modified sugars can be utilized to improve oligonucleotide activities. Those skilled in the art appreciate that, unless specified otherwise, carbon atoms of sugars with indicated connections (e.g., the 5'- and/or 3'-carbons) typically bond to −OH (e.g., when at the ends of oligonucleotides) and/or oxygen atoms which bond to linkage phosphorus atoms in internucleotidic linkages (see, e.g., various oligonucleotides in the Tables). Those skilled in the art appreciate that, unless specified otherwise, oxygen atoms bonded to carbon atoms of sugars with indicated connections herein may be considered part of a sugar if so desired, and may also be considered part of an internucleotidic linkage if so desired.

[00755] Among other things, the present disclosure demonstrates that various non-natural RNA sugars, such as natural DNA sugar, various modified sugars, etc., may be utilized in accordance with the present disclosure. For example, one or more natural DNA sugars can be tolerated at various positions. In some embodiments, incorporation of one or more natural DNA sugars provides increased levels of editing, or increased levels of editing by ADAR1 (p110, p150 or both), ADAR2, or both. In some embodiments, editing by ADAR1 is improved. In some embodiments, one or more sugars of N_{-3}, N_{-1}, N_1, N_4, N_5, N_7, N_8, N_{10}, N_{12}, N_{13}, N_{14}, N_{15}, N_{16}, N_{17}, N_{18}, N_{20}, and N_{21} is independently a natural DNA sugar (-(e.g., N_{-1}): counting from N_0 to the 3'-end of an oligonucleotide; + or just a number (e.g., N_1): counting from N_0 to the 5'-end of an oligonucleotide; each N_{NZ} is independently a nucleoside, wherein NZ is an integer from, e.g., about -100, -90, -80, -70, -60, -50, -40, -30, -20, -10, -9, -8, -7, -6, -5, -4, etc. to). In some embodiments, one or more sugars of N_{-3}, N_{-1}, N_0, N_1, N_4, N_5, N_7, N_8, N_{10}, N_{12}, N_{13}, N_{14}, N_{15}, N_{16}, N_{17}, N_{18}, N_{20}, and N_{21} is independently a natural DNA sugar. In some embodiments, one or more sugars of N_{-1}, N_5, N_{11}, N_{12} and N_{20} are independently a natural DNA sugar. In some embodiments, a sugar of N_{-1} is a natural DNA sugar. In some embodiments, a sugar of N_0 is a natural DNA sugar. In some embodiments, a sugar of N_1 is a natural DNA sugar. In some embodiments, a sugar of N_5 is a natural DNA sugar. In some embodiments, a sugar of N_{11} is a natural DNA sugar. In some embodiments, a sugar of N_{12} is a natural DNA sugar. In some embodiments, modified sugars are tolerated at one or more positions. In some embodiments, 2'-modified sugars, e.g., 2'-F and/or 2'-OR modified sugars are utilized at one or more or a majority of positions, wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl). In some embodiments, modified sugars are utilized at one or more or a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3'. In some embodiments, 2'-OR modified sugars are utilized at one or more or a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3' wherein R is optionally substituted C_{1-6} aliphatic (e.g., methyl). In some embodiments, modified sugars are utilized at one or more or a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3' and one or more 2'-F modified sugars, natural DNA sugars and/or natural RNA sugars are utilized in 5'-$N_1N_0N_{-1}$-3'. In some embodiments, modified sugars are utilized at one or more or a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3' and each sugar of 5'-$N_1N_0N_{-1}$-3' is independently a 2'-F modified sugar, a natural DNA sugar or a natural RNA sugar. In some embodiments, modified sugars are utilized at one or more or a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3' and each sugar of 5'-$N_1N_0N_{-1}$-3' is independently a 2'-F modified sugar or a natural DNA sugar. In some embodiments, modified sugars are utilized at one or more or

a majority of or all positions out of 5'-$N_1N_0N_{-1}$-3' and each sugar of 5'-$N_1N_0N_{-1}$-3' is independently a natural DNA sugar. In some embodiments, modified sugars, e.g., 2'-OR modified sugars (wherein R is optionally substituted C_{1-6} alkyl) provide increased levels of editing, or increased levels of editing by ADAR1 (p110, p150 or both), ADAR2, or both. In some embodiments, editing by ADAR2 is improved. In some embodiments, a modified sugar is a bicyclic sugar (e.g., a LNA sugar, a cEt sugar, etc.). In some embodiments, a bicyclic sugar may be utilized at one or more or all positions where a 2'-OR sugar is utilized, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, 2'-OR is 2'-OMe. In some embodiments, 2'-OR is 2'-MOE. In some embodiments, a majority is at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% (e.g., 55%-100%, 60%-100%, 70-100%, 75%-100%, 80%-100%, 90%-100%, 95%-100%, 60%-95%, 70%-95%, 75-95%, 80-95%, 85-95%, 90-95%, 51%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, or 99%, etc.

[00756] In some embodiments, a sugar of N_{24} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{23} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{22} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{19} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{17} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{13} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{12} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{11} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_9 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_8 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_0 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{-2} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{-3} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{-4} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a sugar of N_{-5} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

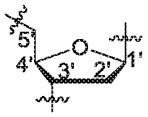
[00757] In some embodiments, a sugar of N_{24} is m1d. In some embodiments, a sugar of N_{16} is m1d. In some embodiments, a sugar of N_{15} is m1d. In some embodiments, a sugar of N_9 is m1d. In some embodiments, a sugar of N_7 is m1d. In some embodiments, a sugar of a second nucleoside from the 5'-end of the oligonucleotide is m1d. In some embodiments, a sugar of a 9th nucleoside from the 5'-end of the oligonucleotide is m1d. In some embodiments, a sugar of a 10th nucleoside from the 5'-end of the oligonucleotide is m1d. In some embodiments, a sugar of an 16th nucleoside from the 5'-end of the oligonucleotide is m1d. In some embodiments, a sugar of a 18th nucleoside from the 5'-end of the oligonucleotide is m1d.

[00758] In some embodiments, one or more (e.g., 1-10, 1, 2, 3, 4, or 5, etc.) of the first several (e.g., 1-10,

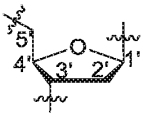
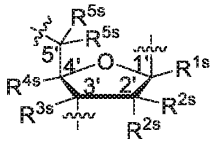
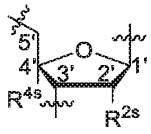
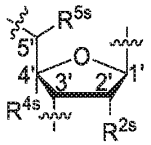
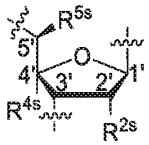
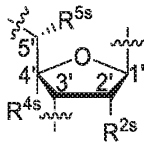
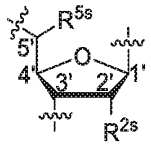
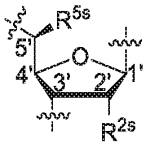
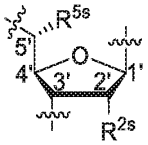
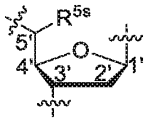
1, 2, 3, 4, or 5, etc.) sugars (unless otherwise specified, from the 5'-end) of a provided oligonucleotide or of a first domain are independently modified sugars. In some embodiments, each of the first several sugars is independently a modified sugar. In some embodiments, the first one, two or three sugars of a provided oligonucleotide or of a first domain are independently modified sugars. In some embodiments, the first sugar is a modified sugar. In some embodiments, the first two sugars are independently modified sugars. In some embodiments, the first three sugars are independently modified sugars (e.g., WV-27458). In some embodiments, a modified sugar is a bicyclic sugar. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, each modified sugar is independently a 2'-modified sugar. In some embodiments, a modified sugar is a 2'-OMe modified sugar. In some embodiments, each modified sugar is a 2'-OMe modified sugar. In some embodiments, a modified sugar is a 2'-MOE modified sugar. In some embodiments, each modified sugar is a 2'-MOE modified sugar. In some embodiments, each modified sugar is independently a 2'-OMe or 2'-MOE modified sugar.

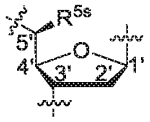
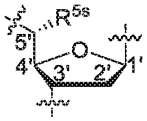
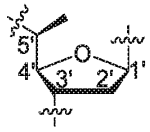
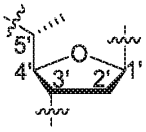
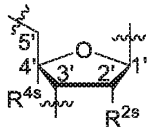
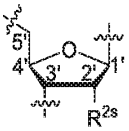
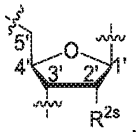
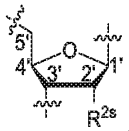
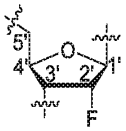
[00759] In some embodiments, one or more (e.g., 1-10, 1, 2, 3, 4, or 5, etc.) of the last several (e.g., 1-10, 1, 2, 3, 4, or 5, etc.) sugars (unless otherwise specified, from the 5'-end) of a provided oligonucleotide or of a second domain or a third subdomain are independently modified sugars. In some embodiments, each of the last several sugars is independently a modified sugar. In some embodiments, the last one, two or three sugars of a provided oligonucleotide or of a second domain or a third subdomain are independently modified sugars. In some embodiments, the last sugar is a modified sugar. In some embodiments, the last two sugars are independently modified sugars. In some embodiments, the last three sugars are independently modified sugars. In some embodiments, the last four sugars are independently modified sugars (e.g., WV-27458). In some embodiments, a modified sugar is a bicyclic sugar. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, each modified sugar is independently a 2'-modified sugar. In some embodiments, a modified sugar is a 2'-OMe modified sugar. In some embodiments, each modified sugar is a 2'-OMe modified sugar. In some embodiments, a modified sugar is a 2'-MOE modified sugar. In some embodiments, each modified sugar is a 2'-MOE modified sugar. In some embodiments, each modified sugar is independently a 2'-OMe or 2'-MOE modified sugar.

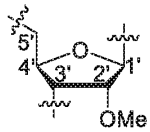
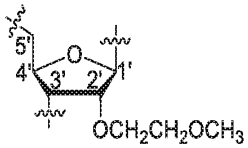
[00760] Sugars can be bonded to internucleotidic linkages at various positions. As non-limiting examples, internucleotidic linkages can be bonded to the 2', 3', 4' or 5' positions of sugars. In some embodiments, as most commonly in natural nucleic acids, an internucleotidic linkage connects with one sugar at the 5' position and another sugar at the 3' position unless otherwise indicated.

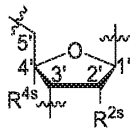
[00761] In some embodiments, a sugar is an optionally substituted natural DNA or RNA sugar. In some embodiments, a sugar is optionally substituted 

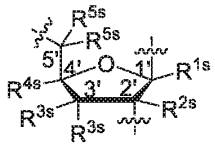
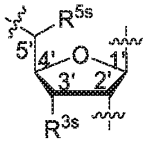
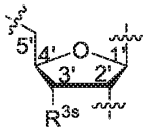
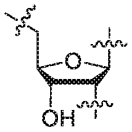
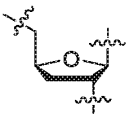
. In some embodiments, the 2' position is

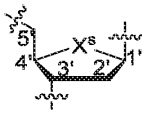
optionally substituted. In some embodiments, a sugar is . In some embodiments, a sugar has the structure of  or , wherein each of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s} is independently −H, a suitable substituent or suitable sugar modification (e.g., those described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the substituents, sugar modifications, descriptions of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s}, and modified sugars of each of which are independently incorporated herein by reference). In some embodiments, each of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s} is independently R^s, wherein each R^s is independently −F, −Cl, −Br, −I, −CN, $-N_3$, −NO, $-NO_2$, $-L^s-R'$, $-L^s-OR'$, $-L^s-SR'$, $-L^s-N(R')_2$, $-O-L^s-OR'$, $-O-L^s-SR'$, or $-O-L^s-N(R')_2$, wherein each R' is independently as described herein, and each L^s is independently a covalent bond or optionally substituted bivalent C_{1-6} aliphatic or heteroaliphatic having 1-4 heteroatoms; or two R^s are taken together to form a bridge $-L^s-$. In some embodiments, R' is optionally substituted C_{1-10} aliphatic. In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of .

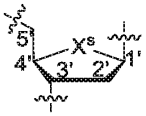
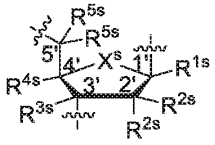
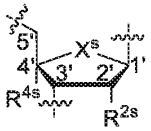
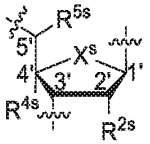
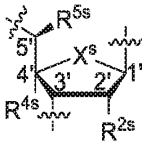
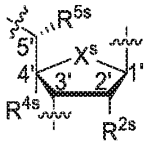
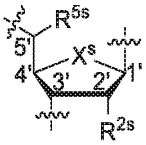
In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, R^{5s} is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{5s} is optionally substituted C_{1-6} alkyl. In some embodiments, R^{5s} is optionally substituted methyl. In some embodiments, R^{5s} is methyl. In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . Various such sugars are utilized in Table 1 and Table 1A. In some embodiments, a sugar has the structure of . In some embodiments, a 2'-modified sugar has the structure of , wherein R^{2s} is a 2'-modification. In some embodiments, a sugar has the structure of , wherein R^{2s} is −H, halogen, or −OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{2s} is −H. In some embodiments, R^{2s} is −F. In some embodiments, R^{2s} is −OMe. In some embodiments, a modified nucleoside is mA, mT, mC, m5mC, mG, mU, etc., in which R^{2s} is −OMe. In some embodiments, R^{2s} is $-OCH_2CH_2OMe$. In some embodiments, a modified nucleoside is Aeo, Teo, Ceo, m5Ceo, Geo, Ueo, etc., in which R^{2s} is $-OCH_2CH_2OMe$. In some embodiments, R^{2s} is $-OCH_2CH_2OH$. In some embodiments, an oligonucleotide comprises a 2'-F modified sugar having the structure of  (e.g., as in fA, fT, fC, f5mC, fG, fU, etc. or indicated by [fl2r]). In some embodiments, an oligonucleotide comprises

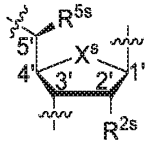
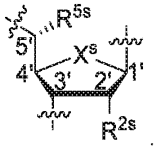
a 2'-OMe modified sugar having the structure of  (e.g., as in mA, mT, mC, m5mC, mG, mU, etc. or indicated by m). In some embodiments, an oligonucleotide comprises a 2'-MOE modified sugar having the structure of  (e.g., as in Aeo, Teo, Ceo, m5Ceo, Geo, Ueo, etc. or indicated by [moe]).

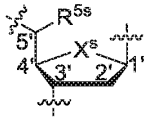
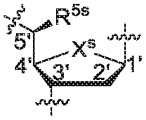
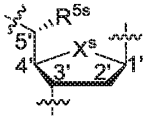
[00762] In some embodiments, a sugar has the structure of , wherein R^{2s} and R^{4s} are taken together to form $-L^s-$, wherein L^s is a covalent bond or optionally substituted bivalent C_{1-6} aliphatic or heteroaliphatic having 1-4 heteroatoms. In some embodiments, each heteroatom is independently selected from nitrogen, oxygen or sulfur). In some embodiments, L^s is optionally substituted C2–O–CH_2–C4. In some embodiments, L^s is C2–O–CH_2–C4. In some embodiments, L^s is C2–O–(*R*)-CH(CH_2CH_3)–C4. In some embodiments, L^s is C2–O–(*S*)-CH(CH_2CH_3)–C4.

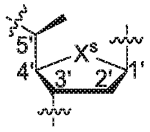
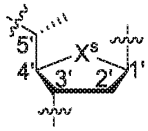
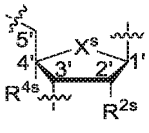
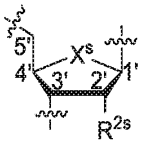
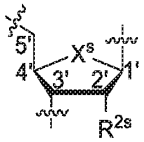
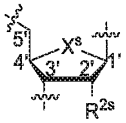
[00763] In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, R^{5s} is –H. In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, R^{3s} is –OH. In some embodiments, R^{3s} is –H. In some embodiments, a sugar is . In some embodiments, a sugar is .

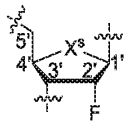
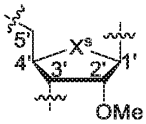
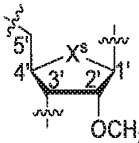
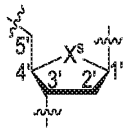
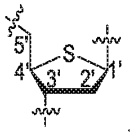
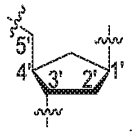


[00764] In some embodiments, a sugar is optionally substituted , wherein X^s is –S–, –Se–, or optionally substituted $-CH_2-$. In some embodiments, the 2' position is optionally substituted. In some embodiments, a sugar is  . In some embodiments, a sugar has the structure of  or  , wherein each of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s} is independently –H, a suitable substituent or suitable sugar modification (e.g., those described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the substituents, descriptions of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s}, and modified sugars of each of which are independently incorporated herein by reference). In some embodiments, each of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s} is independently R^s, wherein each R^s is independently –F, –Cl, –Br, –I, –CN, $-N_3$, –NO, $-NO_2$, $-L^s-R'$, $-L^s-OR'$, $-L^s-SR'$, $-L^s-N(R')_2$, $-O-L^s-OR'$, $-O-L^s-SR'$, or $-O-L^s-N(R')_2$, wherein each R' is independently as described herein, and each L^s is independently a covalent bond or optionally substituted bivalent C_{1-6} aliphatic or heteroaliphatic having 1-4 heteroatoms; or two R^s are taken together to form a bridge $-L^s-$. In some embodiments, R' is optionally substituted C_{1-10} aliphatic. In some embodiments, a sugar has the structure of  . In some embodiments, a sugar has the structure of  . In some embodiments, a sugar has the structure of  . In some embodiments, a sugar has the structure of  . In some embodiments, a

sugar has the structure of . In some embodiments, a sugar has the structure of .

In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, R^{5s} is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{5s} is optionally substituted C_{1-6} alkyl. In some embodiments, R^{5s} is optionally substituted methyl. In some embodiments, R^{5s} is methyl.

In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . In some embodiments, a sugar has the structure of . Various such sugars are utilized in Table 1 and Table 1A. In some embodiments, a sugar has the structure of . In some embodiments, a 2'-modified sugar has the structure of , wherein R^{2s} is a 2'-modification. In some embodiments, a sugar has the structure of , wherein R^{2s} is −H, halogen, or −OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{2s} is −H. In some embodiments, R^{2s} is −F. In some embodiments, R^{2s} is −OMe. In some embodiments, R^{2s} is $-OCH_2CH_2OMe$. In some embodiments, R^{2s} is $-OCH_2CH_2OH$. In some embodiments, a modified sugar has the structure of


. In some embodiments, a modified sugar has the structure of 
. In some embodiments, a modified sugar having the structure of 
. In some embodiments, a modified sugar having the structure of 
. In some embodiments, X^s is $-S-$. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$. In some embodiments, a modified sugar having the structure of 
. In some embodiments, a modified sugar having the structure of 
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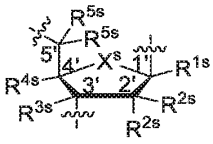
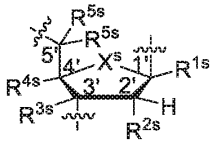
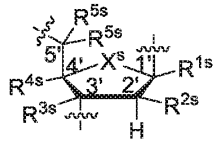
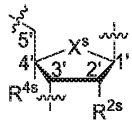
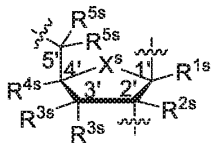
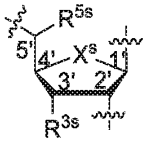
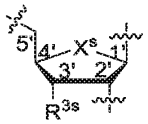
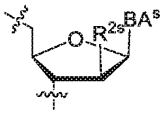
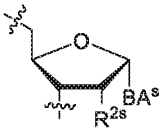
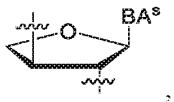
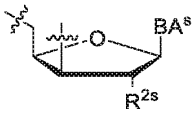
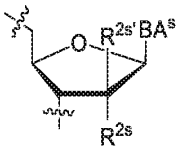
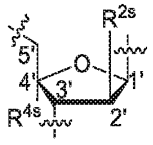
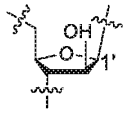
[00765] In some embodiments, a sugar has the structure of 
, 
, or 
, wherein each R^{2s} is independently $-H$, $-F$, $-OH$ or $-OR^{ak}$, wherein R^{ak} is optionally substituted C_{1-6} aliphatic, and each of the other variables is independently as described herein. In some embodiments, each of R^{1s}, R^{3s}, R^{4s}, and R^{5s} is independently $-H$. In some embodiments, each of R^{1s}, R^{3s} and R^{4s}, and one of R^{5s}, are independently $-H$, and the other R^{5s} is independently C_{1-6} aliphatic. In some embodiments, an occurrence of R^{5s} is C_{1-6} aliphatic, e.g., methyl. In some embodiments, R^{2s} is $-H$. In some embodiments, R^{2s} is $-F$. In some embodiments, R^{2s} is $--OR^{ak}$. In some embodiments, R^{2s} is $-OMe$. In some embodiments, R^{2s} is $-OCH_2CH_2CH_3$. In some embodiments, at least one occurrence of R^{2s} is $-H$. In some embodiments, at least one occurrence of R^{2s} is not $-H$. In some embodiments, X^s is $-O-$. In some embodiments, X^s is $-S-$. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$.

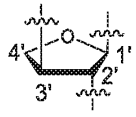
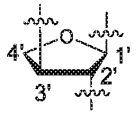
[00766] In some embodiments, a sugar has the structure of , wherein R^{2s} and R^{4s} are taken together to form $-L^s-$, wherein L^s is a covalent bond or optionally substituted bivalent C_{1-6} aliphatic or heteroaliphatic having 1-4 heteroatoms. In some embodiments, each heteroatom is independently selected from nitrogen, oxygen or sulfur). In some embodiments, L^s is optionally substituted C2–O–CH_2–C4. In some embodiments, L^s is C2–O–CH_2–C4. In some embodiments, L^s is C2–O–(*R*)-CH(CH_2CH_3)–C4. In some embodiments, L^s is C2–O–(*S*)-CH(CH_2CH_3)–C4. In some embodiments, X^s is –S–. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$. In some embodiments, X^s is –Se–.

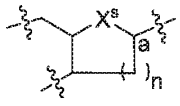
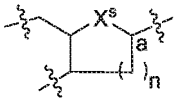
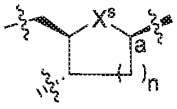
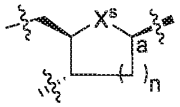
[00767] In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, R^{5s} is –H. In some embodiments, a sugar has the structure of , wherein each variable is independently as described herein. In some embodiments, R^{3s} is –OH. In some embodiments, R^{3s} is –H. In some embodiments, X^s is –S–. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$.

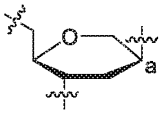
[00768] In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein BA^s is –H or an optionally substituted or protected nucleobase (e.g., BA), and R^{2s} is as described herein. In some embodiments, R^{2s} is –OH, halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, BA^s is –H. In some embodiments, BA^s is an optionally substituted or protected nucleobase. In some embodiments, BA^s is BA. In some embodiments, R^{2s} is –F. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is independently as described herein. In some embodiments, R^{2s} is –H, –OH,

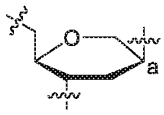
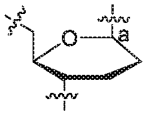
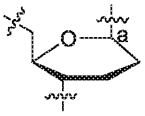
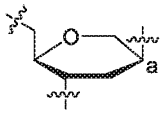
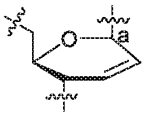
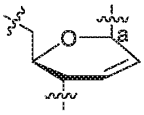
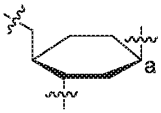
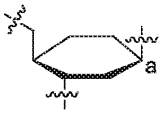
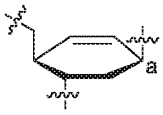
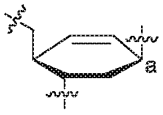
halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, R^{2s} is –H. In some embodiments, R^{2s} is –F. In some embodiments, a nucleoside comprising a modified sugar has the structure of , wherein each variable is as described herein. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is independently as described herein. In some embodiments, R^{2s} is –H, –OH, halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, R^{2s} is –H. In some embodiments, R^{2s} is –F. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein $R^{2s'}$ is R^s, and each of R^s, R^{2s} and BA^s is independently as described herein. In some embodiments, each of R^{2s} and $R^{2s'}$ is independently –H, –OH, halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, R^{2s} is –H. In some embodiments, R^{2s} is –OH. In some embodiments, R^{2s} is halogen. In some embodiments, R^{2s} is –F. In some embodiments, R^{2s} is optionally substituted C_1-C_6 alkoxy. In some embodiments, $R^{2s'}$ is –H. In some embodiments, $R^{2s'}$ is –OH. In some embodiments, $R^{2s'}$ is halogen. In some embodiments, $R^{2s'}$ is –F. In some embodiments, $R^{2s'}$ is optionally substituted C_1-C_6 alkoxy. In some embodiments, BA^s is –H. In some embodiments, BA^s is an optionally substituted or protected nucleobase. In some embodiments, BA^s is BA. In some embodiments, nucleobases such as BA are optionally substituted or protected for oligonucleotide synthesis. Certain such nucleosides including sugars and nucleobases and uses thereof are described in WO 2020/154342. In some embodiments, an oligonucleotide comprises arabinoside, 2'-deoxy-2'-fluoro-arabinoside, 2'-OR arabinoside, adeoxycytidine, DNA-abasic, RNA-abasic, or 2'-OR abasic, wherein R is not hydrogen (e.g., optionally substituted C_{1-6} aliphatic). In some embodiments, 2'-OR is 2'-OMe. In some embodiments, 2'-OR is 2'-MOE. In some embodiments, an oligonucleotide comprises 2'-O-methyl-arabinocytidine (amC). In some embodiments, oligonucleotides comprise such nucleosides. In some embodiments, monomers comprise such nucleosides. In some embodiments, phosphoramidites comprise such nucleosides (in some embodiments, one connecting site (e.g., a $-CH_2-$ connecting site) is bonded to an optionally substituted –OH, e.g., (–ODMTr), and one connecting site (e.g., a ring connecting site) is bonded to O which is also bonded to P of a phosphoramidite). In some embodiments, one or more or each of a 5' immediate nucleoside (e.g., N_1), an opposite nucleoside (N_0) and a 3' immediate nucleoside (e.g., N_{-1}) is independently such a nucleoside. In some embodiments, 5'-$N_1N_0N_{-1}$-3' is amCCA. In some embodiments, a

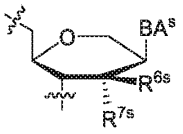
sugar has the structure of , wherein each variable is as described herein and C1' is bonded to a nucleobase. In some embodiments, a sugar is an arabinose. In some embodiments, a sugar has the structure of , wherein C1' is bonded to a nucleobase.

[00769] In some embodiments, a sugar is optionally substituted , wherein a nucleobase is bonded at position 1'. In some embodiments, a sugar is , wherein a nucleobase is bonded at position 1'.

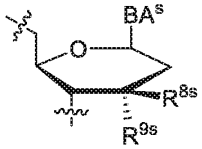
[00770] In some embodiments, a sugar is optionally substituted , wherein position a is bonded to a nucleobase, X^s is $-O-$, $-S-$, $-Se-$ or optionally substituted $-CH_2-$. In some embodiments, a sugar is . In some embodiments, a sugar is optionally substituted , wherein position a is bonded to a nucleobase, X^s is $-O-$, $-S-$, $-Se-$ or optionally substituted $-CH_2-$. In some embodiments, a sugar is . In some embodiments, X^s is $-O-$. In some embodiments, X^s is $-S-$. In some embodiments, X^s is $-Se-$. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$. In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3.

[00771] In some embodiments, a modified sugar comprises an optionally substituted 6-membered ring having 0-1 oxygen atom. In some embodiments, a modified sugar comprises an optionally substituted 6-membered ring having an oxygen atom. For example, in some embodiments, a modified sugar has the structure of optionally substituted , wherein position a is bonded to a nucleobase. In some

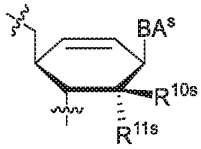
embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. in some embodiments, a modified sugar has the structure of optionally substituted , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of optionally substituted , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of optionally substituted , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of optionally substituted , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a nucleoside comprising a modified sugar has the structure of



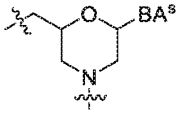
or a salt form thereof, wherein each of R^{6s} and R^{7s} is independently R^s, BA^s is –H or an optionally substituted or protected nucleobase (e.g., BA), and R^s is independently as described herein. In some embodiments, R^{6s} is –H, –OH or halogen, and R^{7s} is –H, –OH, halogen or optionally substituted C_1-C_6 alkoxy. In some embodiments, BA^s is –H. In some embodiments, BA^s is an optionally substituted or protected nucleobase. In some embodiments, BA^s is BA. In some embodiments, a nucleoside comprising a modified sugar has the structure of



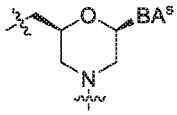
or a salt form thereof, wherein each of R^{8s} and R^{9s} is independently R^s, and each of R^s and BA^s is independently as described herein. In some embodiments, R^{8s} is –H or halogen, and R^{9s} is –H, –OH, halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, a nucleoside comprising a modified sugar has the structure of



or a salt form thereof, wherein each of R^{10s} and R^{11s} is independently R^s, and each of R^s and BA^s is independently as described herein. In some embodiments, R^{10s} is –H or halogen, and R^{11s} is –H, –OH, halogen, or optionally substituted C_1-C_6 alkoxy. In some embodiments, a nucleoside comprising a modified sugar has the structure of

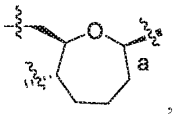
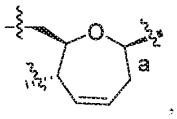
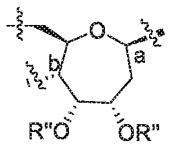
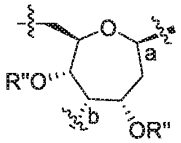
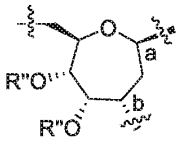


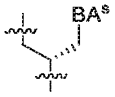
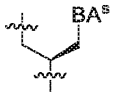
or a salt form thereof, wherein BA^s is as described herein. In some embodiments, a nucleoside comprising a modified sugar has the structure of

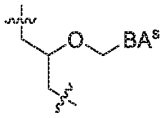


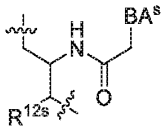
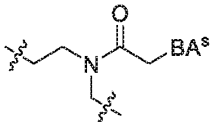
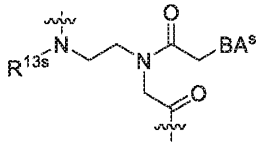
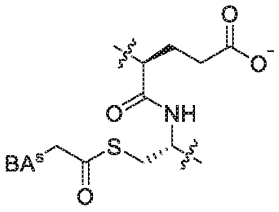
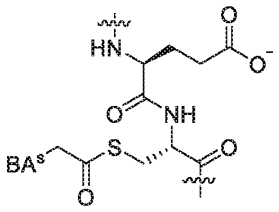
or a salt form thereof, wherein BA^s is as described herein. Those skilled in the art appreciate that in some embodiments, the nitrogen may be directly bonded to linkage phosphorus. In some embodiments, a halogen is –F. In some embodiments, BA^s is –H. In some embodiments, BA^s is an optionally substituted or protected nucleobase. In some embodiments, BA^s is BA. In some embodiments, nucleobases such as BA are optionally substituted or protected for oligonucleotide synthesis. In some embodiments, an oligonucleotide comprises alpha-homo-DNA, beta-homo-DNA moieties. In some embodiments, an oligonucleotide comprises an alpha- or beta-homo-DNA sugar. In some embodiments, an oligonucleotide comprises an alpha-homo-DNA sugar. In some embodiments, an oligonucleotide comprises a beta-homo-DNA sugar. Certain such nucleosides including sugars and nucleobases and uses thereof are described in WO 2020/154343. In some embodiments,

oligonucleotides comprise such nucleosides. In some embodiments, monomers comprise such nucleosides. In some embodiments, phosphoramidites comprise such nucleosides (in some embodiments, one connecting site (e.g., a $-CH_2-$ connecting site) is bonded to an optionally substituted $-OH$, e.g., $-ODMTr$, and one connecting site (e.g., a ring connecting site) is bonded to P of a phosphoramidite (e.g., when the connecting ring atom is N) or to O which is also bonded to P of a phosphoramidite(e.g., when the connecting ring atom is C)). In some embodiments, one or more or each of a 5' immediate nucleoside (e.g., N_1), an opposite nucleoside (N_0) and a 3' immediate nucleoside (e.g., N_{-1}) is independently such a nucleoside.

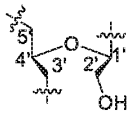
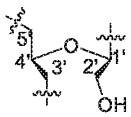
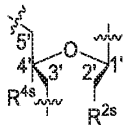
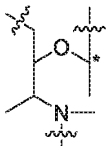
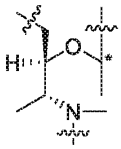
[00773] In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase, position b is bonded to an internucleoside linkage and R'' is $-H$ or optionally substituted C_{1-6} aliphatic. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase, position b is bonded to an internucleoside linkage and R'' is $-H$ or C_{1-6} aliphatic. In some embodiments, a modified sugar has the structure of , wherein position a is bonded to a nucleobase, position b is bonded to an internucleoside linkage and R'' is $-H$ or C_{1-6} aliphatic. In some embodiments, R" is methyl.

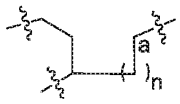
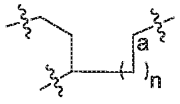
[00774] In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is as described herein. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is as described herein. In some embodiments, a nucleoside comprising a modified sugar has the structure of



or a salt form thereof, wherein each variable is as described herein. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein R^{12s} is R^s, and each of R^s and BA^s is independently as described herein. In some embodiments, R^{12s} is −H, −OH, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} heteroalkyl, or optionally substituted C_{1-6} alkoxy. In some embodiments, a halogen is −F. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is as described herein. In some embodiments, a nucleotide comprising a modified sugar has the structure of  or a salt form thereof, wherein R^{13s} is R^s, and each of R^s and BA^s is independently as described herein. In some embodiments, R^{13s} is −H or optionally substituted C_1-C_6 alkyl. In some embodiments, a nucleoside comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is as described herein. In some embodiments, a nucleotide comprising a modified sugar has the structure of  or a salt form thereof, wherein each variable is as described herein. In some embodiments, a linkage is an amide linkage. In some embodiments, BA^s is −H. In some embodiments, BA^s is an optionally substituted or protected nucleobase. In some embodiments, BA^s is BA. In some embodiments, nucleobases such as BA are optionally substituted or protected for oligonucleotide synthesis. Certain such nucleosides and nucleotides including sugars and nucleobases and uses thereof are described in WO 2020/154344. In some embodiments, oligonucleotides

comprise such nucleosides. In some embodiments, oligonucleotides comprise such nucleosides (in some embodiments, one connecting site (e.g., a $-CH_2-$ connecting site) is bonded to an optionally substituted $-OH$, e.g., ($-ODMTr$), and one connecting site (e.g., a ring connecting site) is bonded to O which is also bonded to P of a phosphoramidite. In some embodiments, one or more or each of a 5' immediate nucleoside (e.g., N_1), an opposite nucleoside (N_0) and a 3' immediate nucleoside (e.g., N_{-1}) is independently such a nucleoside.

[00775] In some embodiments, a sugar is an acyclic sugar, e.g. a UNA sugar. In some embodiments, a sugar is optionally substituted . In some embodiments, the 2' position is optionally substituted. In some embodiments, a sugar is . In some embodiments, a sugar has the structure of . In some embodiments, R^{2s} is $-OH$. In some embodiments, a sugar is , wherein "*" indicates the carbon atom bonded to a nucleobase. In some embodiments, a sugar is , wherein "*" indicates the carbon atom bonded to a nucleobase. In some embodiments, the carbon atom bonded to a nitrogen atom of a nucleobase and is of *R* configuration (e.g., sm18). In some embodiments, an oligonucleotide comprises a sugar described herein.

[00776] In some embodiments, a sugar is optionally substituted , wherein position a is bonded to a nucleobase, X^s is $-O-$, $-S-$, $-Se-$ or optionally substituted $-CH_2-$. In some embodiments, a sugar is . In some embodiments, X^s is $-O-$. In some embodiments, X^s is $-S-$. In some embodiments, X^s is $-Se-$. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$. In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3.

[00777] In some embodiments, a sugar is connected not through 5' and 3' positions. Those skilled in the art appreciate that for such sugars, 5' can refer to the side/direction toward 5'-end of an oligonucleotide, and

3' can refer to the side/direction toward to 3'-end of an oligonucleotide.

[00778] In some embodiments, each of R^{1s}, R^{2s}, R^{3s}, R^{4s}, and R^{5s} is independently R^s, wherein R^s is independently −H, halogen, −CN, $-N_3$, −NO, $-NO_2$, $-L^s-R'$, $-L^s-Si(R')_3$, $-L^s-OR'$, $-L^s-SR'$, $-L^s-N(R')_2$, $-O-L^s-R'$, $-O-L^s-Si(R)_3$, $-O-L^s-OR'$, $-O-L^s-SR'$, or $-O-L^s-N(R')_2$; wherein L^s is L^B as described herein, and each other variable is independently as described herein. In some embodiments, each of R^{1s} and R^{2s} is independently R^s. In some embodiments, R^s is −H. In some embodiments, R^s is not −H. In some embodiments, L^s is a covalent bond. In some embodiments, each of R^{2s} and R^{4s} are independently −H, −F, −OR, $-N(R)_2$. In some embodiments, R^{2s} is −H, −F, −OR, $-N(R)_2$. In some embodiments, R^{4s} is −H. In some embodiments, R^{2s} and R^{4s} form $2'-O-L^s-$, wherein L^s is optionally substituted C_{1-6} alkylene. In some embodiments, L^s is optionally substituted $-CH_2-$. In some embodiments, L^s is optionally substituted $-CH_2-$.

[00779] In some embodiments, R is hydrogen. In some embodiments, R is not hydrogen. In some embodiments, R is an optionally substituted group selected from C_{1-10} aliphatic, C_{1-10} heteroaliphatic having 1-10 heteroatoms independently selected from oxygen, nitrogen, sulfur, phosphorus and silicon, C_{6-20} aryl, a 5-20 membered heteroaryl ring having 1-10 heteroatoms independently selected from oxygen, nitrogen, sulfur, phosphorus and silicon, and a 3-20 membered heterocyclic ring having 1-10 heteroatoms independently selected from oxygen, nitrogen, sulfur, phosphorus and silicon.

[00780] In some embodiments, R is optionally substituted C_{1-30} aliphatic. In some embodiments, R is optionally substituted C_{1-20} aliphatic. In some embodiments, R is optionally substituted C_{1-15} aliphatic. In some embodiments, R is optionally substituted C_{1-10} aliphatic. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted hexyl, pentyl, butyl, propyl, ethyl or methyl. In some embodiments, R is optionally substituted hexyl. In some embodiments, R is optionally substituted pentyl. In some embodiments, R is optionally substituted butyl. In some embodiments, R is optionally substituted propyl. In some embodiments, R is optionally substituted ethyl. In some embodiments, R is optionally substituted methyl. In some embodiments, R is hexyl. In some embodiments, R is pentyl. In some embodiments, R is butyl. In some embodiments, R is propyl. In some embodiments, R is ethyl. In some embodiments, R is methyl. In some embodiments, R is isopropyl. In some embodiments, R is n-propyl. In some embodiments, R is tert-butyl. In some embodiments, R is sec-butyl. In some embodiments, R is n-butyl. In some embodiments, R is $-(CH_2)_2OCH_3$.

[00781] In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl.

[00782] In some embodiments, R^{2s} is a 2'-modification as described in the present disclosure, and R^{4s} is −H. In some embodiments, R^{2s} is −OR, wherein R is not hydrogen. In some embodiments, R^{2s} is −F. In some embodiments, R^{2s} is −OMe. In some embodiments, R^{2s} is $-OCH_2CH_2CH_3$, e.g., in various X_{eo} utilized in Table 1 or Table 1A (X being m5C, T, G, A, etc.). In some embodiments, R^{2s} is selected from −H, −F, and −OR, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, R^{2s} is selected from −H, −F, and −OMe.

[00783] In some embodiments, a sugar is a bicyclic sugar, e.g., sugars wherein R^{2s} and R^{4s} are taken to

form an optionally substituted ring as described in the present disclosure. In some embodiments, a sugar is selected from LNA sugars, BNA sugars, cEt sugars, etc. In some embodiments, a bridge is between the 2' and 4'-carbon atoms (corresponding to R^{2s} and R^{4s} taken together with their intervening atoms to form an optionally substituted ring as described herein). In some embodiments, a bridge is 2'–L^a–L^b–4', wherein L^a is –O–, –S– or N(R), and L^b is an optionally substituted C_{1-4} bivalent aliphatic chain, e.g., methylene.

[00784] In some embodiments, a sugar is a 2'-OMe, 2'-MOE, 2'-F, a LNA (locked nucleic acid) sugar, an ENA (ethylene bridged nucleic acid) sugar, a BNA(NMe) (Methylamino bridged nucleic acid) sugar, 2'-F ANA (2'-F arabinose), alpha-DNA (alpha-D-ribose), 2'/5' ODN (e.g., 2'/5' linked oligonucleotide), Inv (inverted sugar, e.g., inverted desoxyribose), AmR (Amino-Ribose), ThioR (Thio-ribose), HNA (hexose nucleic acid), CeNA (cyclohexene nucleic acid), or MOR (Morpholino) sugar.

[00785] Those skilled in the art after reading the present disclosure will appreciate that various types of sugar modifications are known and can be utilized in accordance with the present disclosure. In some embodiments, a sugar modification is a 2'-modification (e.g., R^{2s}). In some embodiments, a 2'-modification is 2'-F. In some embodiments, a 2'-modification is 2'-OR, wherein R is not hydrogen. In some embodiments, a 2'-modification is 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 2'-modification is 2'-OR, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a 2'-modification is 2'-OMe. In some embodiments, a 2'-modification is 2'-MOE. In some embodiments, a 2'-modification is –O–L^b– or –L^b–L^b– which connects the 2'-carbon of a sugar moiety to another carbon of a sugar moiety. In some embodiments, a 2'-modification is 2'–O–L^b–4' or 2'–L^b–L^b–4' which connects the 2'-carbon of a sugar moiety to the 4'-carbon of a sugar moiety. In some embodiments, a 2'-modification is S-cEt. In some embodiments, a modified sugar is an LNA sugar. In some embodiments, –L^b– is –$C(R)_2$–. In some embodiments, a 2'-modification is (C2–O–$C(R)_2$–C4), wherein each R is independently as described in the present disclosure. In some embodiments, a 2'-modification is a LNA sugar modification (C2–O–CH_2–C4). In some embodiments, a 2'-modification is (C2–O–CHR–C4), wherein R is as described in the present disclosure. In some embodiments, a 2'-modification is (C2–O–(*R*)-CHR–C4), wherein R is as described in the present disclosure and is not hydrogen. In some embodiments, a 2'-modification is (C2–O–(*S*)-CHR–C4), wherein R is as described in the present disclosure and is not hydrogen. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is unsubstituted C_{1-6} alkyl. In some embodiments, R is methyl. In some embodiments, R is ethyl. In some embodiments, a 2'-modification is (C2–O–CHR–C4), wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 2'-modification is (C2–O–CHR–C4), wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a 2'-modification is (C2–O–CHR–C4), wherein R is methyl. In some embodiments, a 2'-modification is (C2–O–CHR–C4), wherein R is ethyl. In some embodiments, a 2'-modification is (C2–O–(*R*)-CHR–C4), wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 2'-modification is (C2–O–(*R*)-CHR–C4), wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a 2'-modification is (C2–O–(*R*)-CHR–C4), wherein R is methyl. In some embodiments, a 2'-modification is

(C2–O–(*R*)-CHR–C4), wherein R is ethyl. In some embodiments, a 2'-modification is (C2–O–(*S*)-CHR–C4), wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a 2'-modification is (C2–O–(*S*)-CHR–C4), wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a 2'-modification is (C2–O–(*S*)-CHR–C4), wherein R is methyl. In some embodiments, a 2'-modification is (C2–O–(*S*)-CHR–C4), wherein R is ethyl. In some embodiments, a 2'-modification is C2–O–(*R*)-CH(CH_2CH_3)–C4. In some embodiments, a 2'-modification is C2–O–(*S*)-CH(CH_2CH_3)–C4. In some embodiments, a sugar is a natural DNA sugar. In some embodiments, a sugar is a natural RNA sugar. In some embodiments, a sugar is an optionally substituted natural DNA sugar. In some embodiments, a sugar is a natural DNA sugar optionally substituted at 2'. In some embodiments, a sugar is a natural DNA sugar substituted at 2' (2'-modification). In some embodiments, a sugar is a natural DNA sugar modified at 2' (2'-modification).

[00786] In some embodiments, a sugar is an optionally substituted ribose or deoxyribose. In some embodiments, a sugar is an optionally modified ribose or deoxyribose, wherein one or more hydroxyl groups of the ribose or deoxyribose moiety is optionally and independently replaced by halogen, R', $–N(R')_2$, –OR', or –SR', wherein each R' is as described herein. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with halogen, R', $–N(R')_2$, –OR', or –SR', wherein each R' is independently described in the present disclosure. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with halogen. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with one or more –F. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with –OR', wherein each R' is independently described in the present disclosure. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with –OR', wherein each R' is independently optionally substituted C_1–C_6 aliphatic. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with –OR', wherein each R' is independently an optionally substituted C_1–C_6 alkyl. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with –OMe. In some embodiments, a sugar is an optionally substituted deoxyribose, wherein the 2' position of the deoxyribose is optionally substituted with –O–methoxyethyl.

[00787] In some embodiments, provided oligonucleotides comprise one or more modified sugars. In some embodiments, provided oligonucleotides comprise one or more modified sugars and one or more natural sugars.

[00788] Examples of bicyclic sugars include sugars of alpha-L-methyleneoxy (4'-CH_2-O-2') LNA, beta-D-methyleneoxy (4'-CH_2-O-2') LNA, ethyleneoxy (4' -$(CH_2)_2$-O-2') LNA, aminooxy (4' -CH_2-O-N(R)-2') LNA, and oxyamino (4'-CH_2-N(R)-O-2') LNA. In some embodiments, a bicyclic sugar, e.g., a LNA or BNA

sugar, is sugar having at least one bridge between two sugar carbons. In some embodiments, a bicyclic sugar in a nucleoside may have the stereochemical configurations of alpha-L-ribofuranose or beta-D-ribofuranose.

[00789] In some embodiments, a bicyclic sugar may be further defined by isomeric configuration. For example, a sugar comprising a 4'-(CH_2)-O-2' bridge may be in the alpha-L configuration or in the beta-D configuration. In some embodiments, a 4' to 2' bridge is a -L-4'-(CH_2)-O-2', b-D-4'-CH_2-O-2', 4'-(CH_2)$_2$-O-2', 4'-CH_2-O-N(R')-2', 4'-CH_2-N(R')-O-2', 4'-CH(R')-O-2', 4'-CH(CH_3)-O-2', 4'-CH_2-S-2', 4'-CH_2-N(R')-2', 4'-CH_2-CH(R')-2', 4'-CH_2-CH(CH_3)-2', and 4'-(CH_2)$_3$-2', wherein each R' is as described in the present disclosure. In some embodiments, R' is −H, a protecting group or optionally substituted C_1-C_{12} alkyl. In some embodiments, R' is −H or optionally substituted C_1-C_{12} alkyl.

[00790] In some embodiments, a bicyclic sugar is a sugar of alpha-L-methyleneoxy (4'-CH_2-O-2') BNA, beta-D-methyleneoxy (4'-CH_2-O-2') BNA, ethyleneoxy (4'-(CH_2)$_2$-O-2') BNA, aminooxy (4'-CH_2-O-N(R)-2') BNA, oxyamino (4'-CH_2-N(R)-O-2') BNA, methyl(methyleneoxy) (4'-CH(CH_3)-O-2') BNA (also referred to as constrained ethyl or cEt), methylene-thio (4'-CH_2-S-2') BNA, methylene-amino (4'-CH_2-N(R)-2') BNA, methyl carbocyclic (4'-CH_2-CH(CH_3)-2') BNA, propylene carbocyclic (4'-(CH_2)$_3$-2') BNA, or vinyl BNA.

[00791] In some embodiments, a sugar modification is a modification described in US 9006198. In some embodiments, a modified sugar is described in US 9006198. In some embodiments, a sugar modification is a modification described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the sugar modifications and modified sugars of each of which are independently incorporated herein by reference.

[00792] In some embodiments a modified sugar is one described in US 5658873, US 5118800, US 5393878, US 5514785, US 5627053, US 7034133;7084125, US 7399845, US 5319080, US 5591722, US 5597909, US 5466786, US 6268490, US 6525191, US 5519134, US 5576427, US 6794499, US 6998484, US 7053207, US 4981957, US 5359044, US 6770748, US 7427672, US 5446137, US 6670461, US 7569686, US 7741457, US 8022193, US 8030467, US 8278425, US 5610300, US 5646265, US 8278426, US 5567811, US 5700920, US 8278283, US 5639873, US 5670633, US 8314227, US 2008/0039618, US 2009/0012281, WO 2021/030778, WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, or WO 2020/252376.

[00793] In some embodiments, a sugar modification is 2'-OMe, 2'-MOE, 2'-LNA, 2'-F, 5'-vinyl, or S-cEt. In some embodiments, a modified sugar is a sugar of FRNA, FANA, or morpholino. In some embodiments, an oligonucleotide comprises a nucleic acid analog, e.g., GNA, LNA, PNA, TNA, F-HNA (F-THP or 3'-fluoro tetrahydropyran), MNA (mannitol nucleic acid, e.g., Leumann 2002 Bioorg. Med. Chem. 10: 841-854), ANA (anitol nucleic acid), or morpholino, or a portion thereof. In some embodiments, a sugar is as

in flexible nucleic acids or serinol nucleic acids. In some embodiments, a sugar modification replaces a natural sugar with another cyclic or acyclic moiety. Examples of such moieties are widely known in the art, e.g., those used in morpholino, glycol nucleic acids, etc. and may be utilized in accordance with the present disclosure. As appreciated by those skilled in the art, when utilized with modified sugars, in some embodiments internucleotidic linkages may be modified, e.g., as in morpholino, PNA, etc. In some embodiments, a sugar is a (R)-GNA sugar. In some embodiments, a sugar is a (S)-GNA sugar. In some embodiments, a nucleoside having a GNA sugar is utilized as N_{-1}, N_0 and/or N_1. In some embodiments, N_0 is a nucleoside having a GNA sugar. In some embodiments, a sugar is bicyclic sugar. In some embodiments, a sugar is a LNA sugar. In some embodiments, a sugar is an acyclic sugar. In some embodiments, a sugar is a UNA sugar. In some embodiments, a nucleoside having a UNA sugar is utilized as N_{-1}, N_0 and/or N_1. In some embodiments, N_0 is a nucleoside having a UNA sugar. In some embodiments, a nucleoside is abasic. In some embodiments, an abasic sugar is utilized as N_{-1}, N_0 and/or N_1. In some embodiments, N_0 is a nucleoside having an abasic sugar.

[00794] In some embodiments, a sugar is a 6'-modified bicyclic sugar that have either (R) or (S)-chirality at the 6-position, e.g., those described in US 7399845. In some embodiments, a sugar is a 5'-modified bicyclic sugar that has either (R) or (S)-chirality at the 5-position, e.g., those described in US 20070287831.

[00795] In some embodiments, a modified sugar contains one or more substituents at the 2' position (typically one substituent, and often at the axial position) independently selected from –F; $–CF_3$, –CN, $–N_3$, –NO, $–NO_2$, –OR', –SR', or $–N(R')_2$, wherein each R' is independently described in the present disclosure; –O–(C_1–C_{10} alkyl), –S–(C_1–C_{10} alkyl), –NH–(C_1–C_{10} alkyl), or $–N(C_1–C_{10}$ alkyl$)_2$; –O–(C_2–C_{10} alkenyl), –S–(C_2–C_{10} alkenyl), –NH–(C_2–C_{10} alkenyl), or $–N(C_2–C_{10}$ alkenyl$)_2$; –O–(C_2–C_{10} alkynyl), –S–(C_2–C_{10} alkynyl), –NH–(C_2–C_{10} alkynyl), or $–N(C_2–C_{10}$ alkynyl$)_2$; or –O–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), –O–(C_1–C_{10} alkylene)–NH–(C_1–C_{10} alkyl) or –O–(C_1–C_{10} alkylene)–$NH(C_1–C_{10}$ alkyl$)_2$, –NH–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), or $–N(C_1–C_{10}$ alkyl)–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), wherein each of the alkyl, alkylene, alkenyl and alkynyl is independently and optionally substituted. In some embodiments, a substituent is –$O(CH_2)_nOCH_3$, –$O(CH_2)_nNH_2$, MOE, DMAOE, or DMAEOE, wherein n is from 1 to about 10. In some embodiments, a modified sugar is one described in WO 2001/088198; and Martin et al., Helv. Chim. Acta, 1995, 78, 486-504. In some embodiments, a modified sugar comprises one or more groups selected from a substituted silyl group, an RNA cleaving group, a reporter group, a fluorescent label, an intercalator, a group for improving the pharmacokinetic properties of a nucleic acid, a group for improving the pharmacodynamic properties of a nucleic acid, or other substituents having similar properties. In some embodiments, modifications are made at one or more of the 2', 3', 4', or 5' positions, including the 3' position of the sugar on the 3'-terminal nucleoside or in the 5' position of the 5'-terminal nucleoside.

[00796] In some embodiments, the 2'-OH of a ribose is replaced with a group selected from –H, –F; $–CF_3$, –CN, $–N_3$, –NO, $–NO_2$, –OR', –SR', or $–N(R')_2$, wherein each R' is independently described in the present disclosure; –O–(C_1–C_{10} alkyl), –S–(C_1–C_{10} alkyl), –NH–(C_1–C_{10} alkyl), or $–N(C_1–C_{10}$ alkyl$)_2$; –O–(C_2–C_{10} alkenyl), –S–(C_2–C_{10} alkenyl), –NH–(C_2–C_{10} alkenyl), or $–N(C_2–C_{10}$ alkenyl$)_2$; –O–(C_2–C_{10} alkynyl), –S–(C_2–

C_{10} alkynyl), –NH–(C_2–C_{10} alkynyl), or –N(C_2–C_{10} alkynyl)$_2$; or –O–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), –O–(C_1–C_{10} alkylene)–NH–(C_1–C_{10} alkyl) or –O–(C_1–C_{10} alkylene)–NH(C_1–C_{10} alkyl)$_2$, –NH–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), or –N(C_1–C_{10} alkyl)–(C_1–C_{10} alkylene)–O–(C_1–C_{10} alkyl), wherein each of the alkyl, alkylene, alkenyl and alkynyl is independently and optionally substituted. In some embodiments, the 2'–OH is replaced with –H (deoxyribose). In some embodiments, the 2'–OH is replaced with –F. In some embodiments, the 2'–OH is replaced with –OR'. In some embodiments, the 2'–OH is replaced with –OMe. In some embodiments, the 2'–OH is replaced with –OCH_2CH_2OMe.

[00797] In some embodiments, a sugar modification is a 2'-modification. Commonly used 2'-modifications include but are not limited to 2'–OR, wherein R is not hydrogen and is as described in the present disclosure. In some embodiments, a modification is 2'–OR, wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, a modification is 2'–OR, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, a modification is 2'–OMe. In some embodiments, a modification is 2'-MOE. In some embodiments, a 2'-modification is S-cEt. In some embodiments, a modified sugar is an LNA sugar. In some embodiments, a 2'-modification is –F. In some embodiments, a 2'-modification is FANA. In some embodiments, a 2'-modification is FRNA. In some embodiments, a sugar modification is a 5'-modification, e.g., 5'-Me. In some embodiments, a sugar modification changes the size of the sugar ring. In some embodiments, a sugar modification is the sugar moiety in FHNA.

[00798] In some embodiments, a sugar modification replaces a sugar moiety with another cyclic or acyclic moiety. Examples of such moieties are widely known in the art, including but not limited to those used in morpholino (optionally with its phosphorodiamidate linkage), glycol nucleic acids, etc.

[00799] In some embodiments, one or more of the sugars of an oligonucleotide are modified. In some embodiments, a modified sugar comprises a 2'-modification. In some embodiments, each modified sugar independently comprises a 2'-modification. In some embodiments, a 2'-modification is 2'-OR. In some embodiments, a 2'-modification is a 2'-OMe. In some embodiments, a 2'-modification is a 2'-MOE. In some embodiments, a 2'-modification is an LNA sugar modification. In some embodiments, a 2'-modification is 2'-F. In some embodiments, each sugar modification is independently a 2'-modification. In some embodiments, each sugar modification is independently 2'-OR or 2'-F. In some embodiments, each sugar modification is independently 2'-OR or 2'-F, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, each sugar modification is independently 2'-OR or 2'-F, wherein at least one is 2'-F. In some embodiments, each sugar modification is independently 2'-OR or 2'-F, wherein R is optionally substituted C_{1-6} alkyl, and wherein at least one is 2'-OR. In some embodiments, each sugar modification is independently 2'-OR or 2'-F, wherein at least one is 2'-F, and at least one is 2'-OR. In some embodiments, each sugar modification is independently 2'-OR or 2'-F, wherein R is optionally substituted C_{1-6} alkyl, and wherein at least one is 2'-F, and at least one is 2'-OR. In some embodiments, each sugar modification is independently 2'-OR. In some embodiments, each sugar modification is independently 2'-OR, wherein R is optionally substituted C_{1-6} alkyl. In some embodiments, each sugar modification is 2'-OMe. In some embodiments, each

sugar modification is 2'-MOE. In some embodiments, each sugar modification is independently 2'-OMe or 2'-MOE. In some embodiments, each sugar modification is independently 2'-OMe, 2'-MOE, or a LNA sugar.

[00800] Modified sugars include cyclobutyl or cyclopentyl moieties in place of a pentofuranosyl sugar. Representative examples of such modified sugars include those described in US 4,981,957, US 5,118,800, US 5,319,080, or US 5,359,044. In some embodiments, the oxygen atom within the ribose ring is replaced by nitrogen, sulfur, selenium, or carbon. In some embodiments, –O– is replaced with –N(R')–, –S–, –Se– or –C(R')$_2$–. In some embodiments, a modified sugar is a modified ribose wherein the oxygen atom within the ribose ring is replaced with nitrogen, and wherein the nitrogen is optionally substituted with an alkyl group (e.g., methyl, ethyl, isopropyl, etc.).

[00801] A non-limiting example of modified sugars is glycerol, which is part of glycerol nucleic acids (GNAs), e.g., as described in Zhang, R et al., J. Am. Chem. Soc., 2008, 130, 5846-5847; Zhang L, et al., J. Am. Chem. Soc., 2005, 127, 4174-4175 and Tsai CH et al., PNAS, 2007, 14598-14603.

[00802] A flexible nucleic acid (FNA) is based on a mixed acetal aminal of formyl glycerol, e.g., as described in Joyce GF et al., PNAS, 1987, 84, 4398-4402 and Heuberger BD and Switzer C, J. Am. Chem. Soc., 2008, 130, 412-413.

[00803] In some embodiments, an oligonucleotide, and/or a modified nucleoside thereof, comprises a sugar or modified sugar described in: WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the sugars and modified sugars of each of which are independently incorporated herein by reference.

[00804] In some embodiments, one or more hydroxyl group in a sugar is optionally and independently replaced with halogen, R' –N(R')$_2$, –OR', or –SR', wherein each R' is independently described in the present disclosure.

[00805] In some embodiments, a modified nucleoside is any modified nucleoside described in: WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the modified nucleosides of each of which are independently incorporated herein by reference.

[00806] In some embodiments, a sugar modification is 5'-vinyl (R or S), 5'-methyl (R or S), 2'-SH, 2'-F, 2'-OCH_3, 2'-OCH_2CH_3, 2'-OCH_2CH_2F or 2'-$O(CH_2)_{20}CH_3$. In some embodiments, a substituent at the 2' position, e.g., a 2'-modification, is allyl, amino, azido, thio, O-allyl, O-C_1-C_{10} alkyl, OCF_3, OCH_2F, $O(CH_2)_2SCH_3$, $O(CH_2)_2$-O-N(R_m)(R_n), O-CH_2-C(=O)-N(R_m)(R_n), and O-CH_2-C(=O)-N(R_1)-$(CH_2)_2$-N(R_m)(R_n), wherein each allyl, amino and alkyl is optionally substituted, and each of R_1, R_m and R_n is independently R' as described in the present disclosure. In some embodiments, each of R_1, R_m and R_n is independently –H or optionally substituted C_1-C_{10} alkyl.

[00807] In some embodiments, bicyclic sugars comprise a bridge, e.g., $-L^b-L^b-$, $-L-$, etc. between two sugar carbons, e.g., between the 4' and the 2' ribosyl ring carbon atoms. In some embodiments, a bridge is 4'-(CH_2)-O-2' (e.g., LNA sugars), 4'-(CH_2)-S-2', 4'-$(CH_2)_2$-O-2' (e.g., ENA sugars), 4'-CH(R')-O-2' (e.g., 4'-$CH(CH_3)$-O-2', 4'-$CH(CH_2OCH_3)$-O-2', and examples in US 7399845, etc.), 4'-$CH(R')_2$-O-2' (e.g., 4'-$C(CH_3)(CH_3)$-O-2' and examples in WO 2009006478, etc.), 4'-CH_2-N(OR')-2' (e.g., 4'-CH_2-$N(OCH_3)$-2', examples in WO 2008150729, etc.), 4'-CH_2-O-N(R')-2' (e.g., 4'-CH_2-O-$N(CH_3)$-2', examples in US 20040171570, etc.), 4'-CH_2-N(R')-O-2' [e.g., wherein R is -H, C_1-C_{12} alkyl, or a protecting group (e.g., see US 7427672)], 4'-$C(R')_2$-C(H)(R')-2' (e.g., 4'-CH_2-$C(H)(CH_3)$-2', examples in Chattopadhyaya et al., J. Org. Chem., 2009, 74, 118-134, etc.), or 4'-$C(R')_2$-$C(=C(R')_2)$-2' (e.g., 4'-CH_2-$C(=CH_2)$-2', examples in WO 2008154401, etc.).

[00808] In some embodiments, a sugar is a tetrahydropyran or THP sugar. In some embodiments, a modified nucleoside is tetrahydropyran nucleoside or THP nucleoside which is a nucleoside having a six-membered tetrahydropyran sugar substituted for a pentofuranosyl residue in typical natural nucleosides. THP sugars and/or nucleosides include those used in hexitol nucleic acid (HNA), anitol nucleic acid (ANA), mannitol nucleic acid (MNA) (e.g., Leumann, Bioorg. Med. Chem., 2002, 10, 841-854) or fluoro HNA (F-HNA).

[00809] In some embodiments, sugars comprise rings having more than 5 atoms and/or more than one heteroatom, e.g., morpholino sugars which are described in e.g., Braasch et al., Biochemistry, 2002, 41, 4503-4510; US 5698685; US 5166315; US 5185444; US 5034506; etc.).

[00810] As those skilled in the art will appreciate, modifications of sugars, nucleobases, internucleotidic linkages, etc. can and are often utilized in combination in oligonucleotides, e.g., see various oligonucleotides in Table 1 and Table 1A.

[00811] In some embodiments, a nucleoside has a six-membered cyclohexenyl in place of the pentofuranosyl residue in naturally occurring nucleosides. Example cyclohexenyl nucleosides and preparation and uses thereof are described in, e.g., WO 2010036696; Robeyns et al., J. Am. Chem. Soc., 2008, 130(6), 1979-1984; Horvath et al., Tetrahedron Letters, 2007, 48, 3621-3623; Nauwelaerts et al., J. Am. Chem. Soc., 2007, 129(30), 9340-9348; Gu et al., Nucleosides, Nucleotides & Nucleic Acids, 2005, 24(5-7), 993-998; Nauwelaerts et al., Nucleic Acids Research, 2005, 33(8), 2452-2463; Robeyns et al., Acta Crystallographica, Section F: Structural Biology and Crystallization Communications, 2005, F61(6), 585-586; Gu et al., Tetrahedron, 2004, 60(9), 2111-2123; Gu et al., Oligonucleotides, 2003, 13(6), 479-489; Wang et al., J. Org. Chem., 2003, 68, 4499-4505; Verbeure et al., Nucleic Acids Research, 2001, 29(24), 4941-4947; Wang et al., J. Org. Chem., 2001, 66, 8478-82; Wang et al., Nucleosides, Nucleotides & Nucleic Acids, 2001, 20(4-7), 785-788; Wang et al., J. Am. Chem., 2000, 122, 8595-8602; WO 2006047842; WO 2001049687; etc.

[00812] Many monocyclic, bicyclic and tricyclic ring systems are suitable as sugar surrogates (modified sugars) and may be utilized in accordance with the present disclosure. See, e.g., Leumann, Christian J. Bioorg. & Med. Chem., 2002, 10, 841-854. Such ring systems can undergo various additional substitutions to further

enhance their properties and/or activities.

[00813] In some embodiments, a 2'-modified sugar is a furanosyl sugar modified at the 2' position. In some embodiments, a 2'-modification is halogen, −R' (wherein R' is not −H), −OR' (wherein R' is not −H), −SR', $-N(R')_2$, optionally substituted $-CH_2-CH=CH_2$, optionally substituted alkenyl, or optionally substituted alkynyl. In some embodiments, a 2'-modifications is selected from $-O[(CH_2)_nO]_mCH_3$, $-O(CH_2)_nNH_2$, $-O(CH_2)_nCH_3$, $-O(CH_2)_nF$, $-O(CH_2)_nONH_2$, $-OCH_2C(=O)N(H)CH_3$, and $-O(CH_2)_nON[(CH_2)_nCH_3]_2$, wherein each n and m is independently from 1 to about 10. In some embodiments, a 2'-modification is optionally substituted C_1-C_{12} alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkaryl, optionally substituted aralkyl, optionally substituted −O−alkaryl, optionally substituted −O−aralkyl, −SH, $-SCH_3$, −OCN, −Cl, −Br, −CN, −F, $-CF_3$, $-OCF_3$, $-SOCH_3$, $-SO_2CH_3$, $-ONO_2$, $-NO_2$, $-N_3$, $-NH_2$, optionally substituted heterocycloalkyl, optionally substituted heterocycloalkaryl, optionally substituted aminoalkylamino, optionally substituted polyalkylamino, substituted silyl, a reporter group, an intercalator, a group for improving pharmacokinetic properties, a group for improving the pharmacodynamic properties, and other substituents. In some embodiments, a 2'-modification is a 2'-MOE modification (e.g., see Baker et al., J. Biol. Chem., 1997, 272, 11944-12000). In some cases, a 2'-MOE modification has been reported as having improved binding affinity compared to unmodified sugars and to some other modified nucleosides, such as 2'- O-methyl, 2'-O-propyl, and 2'-O-aminopropyl. Oligonucleotides having the 2'-MOE modification have also been reported to be capable of inhibiting gene expression with promising features for in vivo use (see, e.g., Martin, Helv. Chim. Acta, 1995, 78, 486-504; Altmann et al., Chimia, 1996, 50, 168-176; Altmann et al., Biochem. Soc. Trans., 1996, 24, 630-637; and Altmann et al., Nucleosides Nucleotides, 1997, 16, 917-926; etc.).

[00814] In some embodiments, a 2'-modified or 2'-substituted sugar or nucleoside is a sugar or nucleoside comprising a substituent at the 2' position of the sugar which is other than −H (typically not considered a substituent) or −OH. In some embodiments, a 2'-modified sugar is a bicyclic sugar comprising a bridge connecting two carbon atoms of the sugar ring one of which is the 2' carbon. In some embodiments, a 2'-modification is non-bridging, e.g., allyl, amino, azido, thio, optionally substituted −O−allyl, optionally substituted $-O-C_1$-C_{10} alkyl, $-OCF_3$, $-O(CH_2)_2OCH_3$, $2'-O(CH_2)_2SCH_3$, $-O(CH_2)_2ON(R_m)(R_n)$, or $-OCH_2C(=O)N(R_m)(R_n)$, where each R_m and R_n is independently −H or optionally substituted C_1-C_{10} alkyl.

[00815] Certain modified sugars, their preparation and uses are described in US 4981957, US 5118800, US 5319080, US 5359044, US 5393878, US 5446137, US 5466786, US 5514785, US 5519134, US 5567811, US 5576427, US 5591722, US 5597909, US 5610300, US 5627053, US 5639873, US 5646265, US 5670633, US 5700920, US 5792847, US 6600032 and WO 2005121371.

[00816] In some embodiments, a sugar is the sugar of N-methanocarba, LNA, cMOE BNA, cEt BNA, α-L-LNA or related analogs, HNA, Me-ANA, MOE-ANA, Ara-FHNA, FHNA, R-6'-Me-FHNA, S-6'-Me-FHNA, ENA, or c-ANA. In some embodiments, a modified internucleotidic linkage is C3-amide (e.g., sugar

that has the amide modification attached to the C3', Mutisya et al. 2014 Nucleic Acids Res. 2014 Jun 1; 42(10): 6542–6551), formacetal, thioformacetal, MMI [e.g., methylene(methylimino), Peoc'h et al. 2006 Nucleosides and Nucleotides 16 (7-9)], a PMO (phosphorodiamidate linked morpholino) linkage (which connects two sugars), or a PNA (peptide nucleic acid) linkage. In some embodiments, examples of internucleotidic linkages and/or sugars are described in Allerson et al. 2005 J. Med. Chem. 48: 901-4; BMCL 2011 21: 1122; BMCL 2011 21: 588; BMCL 2012 22: 296; Chattopadhyaya et al. 2007 J. Am. Chem. Soc. 129: 8362; Chem. Bio. Chem. 2013 14: 58; Curr. Prot. Nucl. Acids Chem. 2011 1.24.1; Egli et al. 2011 J. Am. Chem. Soc. 133: 16642; Hendrix et al. 1997 Chem. Eur. J. 3: 110; Hyrup et al. 1996 Bioorg. Med. Chem. 4: 5; Imanishi 1997 Tet. Lett. 38: 8735; J. Am. Chem. Soc. 1994, 116, 3143; J. Med. Chem. 2009 52: 10; J. Org. Chem. 2010 75: 1589; Jepsen et al. 2004 Oligo. 14: 130-146; Jones et al. J. Org. Chem. 1993, 58, 2983; Jung et al. 2014 ACIEE 53: 9893; Kodama et al. 2014 AGDS; Koizumi 2003 BMC 11: 2211; Koizumi et al. 2003 Nuc. Acids Res. 12: 3267-3273; Koshkin et al. 1998 Tetrahedron 54: 3607-3630; Kumar et al. 1998 Bioo. Med. Chem. Let. 8: 2219-2222; Lauritsen et al. 2002 Chem. Comm. 5: 530-531; Lauritsen et al. 2003 Bioo. Med. Chem. Lett. 13: 253-256; Lima et al. 2012 Cell 150: 883-894; Mesmaeker et al. Angew. Chem., Int. Ed. Engl. 1994, 33, 226; Migawa et al. 2013 Org. Lett. 15: 4316; Mol. Ther. Nucl. Acids 2012 1: e47; Morita et al. 2001 Nucl. Acids Res. Supp. 1: 241-242; Morita et al. 2002 Bioo. Med. Chem. Lett. 12: 73-76; Morita et al. 2003 Bioo. Med. Chem. Lett. 2211-2226; Murray et al. 2012 Nucl. Acids Res. 40: 6135; Nielsen et al. 1997 Chem. Soc. Rev. 73; Nielsen et al. 1997 J. Chem. Soc. Perkins Transl. 1: 3423-3433; Obika et al. 1997 Tetrahedron Lett. 38 (50): 8735–8; Obika et al. 1998 Tetrahedron Lett. 39: 5401-5404; Obika et al. 2008 J. Am. Chem. Soc. 130: 4886; Obika et al. 2011 Org. Lett. 13: 6050; Oestergaard et al. 2014 JOC 79: 8877; Pallan et al. 2012 Biochem. 51: 7; Pallan et al. 2012 Chem. Comm. 48: 8195-8197; Petersen et al. 2003 TRENDS Biotech. 21: 74-81; Prakash et al. 2010 J. Med. Chem. 53: 1636; Prakash et al. 2015 Nucl. Acids Res. 43: 2993-3011; Prakash et al. 2016 Bioorg. Med. Chem. Lett. 26: 2817-2820; Rajwanshi et al. 1999 Chem. Commun. 1395-1396; Schultz et al. 1996 Nucleic Acids Res. 24: 2966; Seth et al. 2008 Nucl. Acid Sym. Ser. 52: 553; Seth et al. 2009 J. Med. Chem. 52: 10-13; Seth et al. 2010 J. Am. Chem. Soc. 132: 14942; Seth et al. 2010 J. Med. Chem. 53: 8309-8318; Seth et al. 2010 J. Org. Chem. 75: 1569-1581; Seth et al. 2011 BMCL 21: 4690; Seth et al. 2012 Bioo. Med. Chem. Lett. 22: 296-299; Seth et al. 2012 Mol. Ther-Nuc. Acids. 1, e47; Seth et al., Nucleic Acids Symposium Series (2008), 52(1), 553-554; Singh et al. 1998 Chem. Comm. 1247-1248; Singh et al. 1998 J. Org. Chem. 63: 10035-39; Singh et al. 1998 J. Org. Chem. 63: 6078-6079; Sorensen 2003 Chem. Comm. 2130-2131; Starrup et al. 2010 Nucl. Acids Res. 38: 7100; Swayze et al. 2007 Nucl. Acids Res. 35: 687; Ts'o et al. Ann. N. Y. Acad. Sci. 1988, 507, 220; Van Aerschot et al. 1995 Angew. Chem. Int. Ed. Engl. 34: 1338; Vasseur et al. J. Am. Chem. Soc. 1992, 114, 4006; WO 2007090071; WO 2016079181; US 6326199; US 6066500; or US 6440739.

[00817] In some embodiments, an oligonucleotide or a portion thereof (e.g., a domain, a subdomain, etc.) comprise a high level of 2'-F modified sugars, e.g., about 10%-100% (e.g., about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or more, or about 100%) of sugars in an

oligonucleotide or a portion thereof (e.g., a domain, a subdomain, etc.) comprises 2'-F. In some embodiments, about 50% or more of sugars in an oligonucleotide or a portion thereof comprises 2'-F. In some embodiments, about 60% or more of sugars in an oligonucleotide or a portion thereof comprises 2'-F. In some embodiments, about 70% or more of sugars in an oligonucleotide or a portion thereof comprises 2'-F. In some embodiments, about 80% or more of sugars in an oligonucleotide or a portion thereof comprises 2'-F. In some embodiments, about 90% or more of sugars in an oligonucleotide or a portion thereof comprises 2'-F. In some embodiments, an oligonucleotide or a portion thereof also comprises one or more sugars comprising no 2'-F (e.g., sugars comprising no modifications and/or sugars comprising other modifications).

[00818] In some embodiments, no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in an oligonucleotide or a portion thereof (e.g., a domain, a subdomain, etc.) comprises 2'-MOE. In some embodiments, no more than about 50% of sugars in an oligonucleotide or a portion thereof comprises 2'-MOE. In some embodiments, no sugars in an oligonucleotide or a portion thereof comprises 2'-MOE. In some embodiments, no more than 1, 2, 3, 4, or 5 sugars in an oligonucleotide or a portion thereof comprises 2'-MOE.

[00819] Various additional sugars useful for preparing oligonucleotides or analogs thereof are known in the art and may be utilized in accordance with the present disclosure.

Internucleotidic linkages

[00820] Among other things, the present disclosure provides various internucleotidic linkages, including various modified internucleotidic linkages, that may be utilized together with other structural elements, e.g., various sugars as described herein, to provide oligonucleotides and compositions thereof.

[00821] In some embodiments, oligonucleotides comprise base modifications, sugar modifications, and/or internucleotidic linkage modifications. Various internucleotidic linkages can be utilized in accordance with the present disclosure to link units comprising nucleobases, e.g., nucleosides. In some embodiments, provided oligonucleotides comprise both one or more modified internucleotidic linkages and one or more natural phosphate linkages.

[00822] Various internucleotidic linkages may be utilized in oligonucleotides in accordance with the present disclosure. In some embodiments, an oligonucleotide comprises one or more types of internucleotidic linkage. In some embodiments, an oligonucleotide comprises two or more types of internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least three types of internucleotidic linkages. In some embodiments, a linkage contains a linkage phosphorus atom bonded to an oxygen atom which oxygen atom is not bonded to or is not part of a backbone sugar ("a PO linkage", e.g., a natural phosphate linkage). In some embodiments, a linkage contains a linkage phosphorus atom bonded to a sulfur atom which sulfur atom is not bonded to or is not part of a backbone sugar ("a PS linkage", e.g., a phosphorothioate internucleotidic linkage). In some embodiments, a linkage contains a linkage phosphorus atom bonded to a nitrogen atom which nitrogen atom is not bonded to or is not part of a backbone sugar ("a PN linkage", e.g., n001, n006, MsPA, etc.). In

some embodiments, an oligonucleotide comprises one or more PS linkages. In some embodiments, an oligonucleotide comprises one or more PO linkages. In some embodiments, an oligonucleotide comprises one or more PN linkages. In some embodiments, an oligonucleotide comprises one or more PS and one or more PO linkages. In some embodiments, an oligonucleotide comprises one or more PS and one or more PN linkages. In some embodiments, an oligonucleotide comprises one or more PS, one or more PN and one or more PO linkages. In some embodiments, a PS linkage is a phosphorothioate linkage. In some embodiments, each PS linkage is independently a phosphorothioate linkage. In some embodiments, a PO linkage is a natural phosphate linkage. In some embodiments, each PO linkage is independently a natural phosphate linkage. In some embodiments, a PN linkage is a phosphoryl guanidine linkage. In some embodiments, each PN linkage is independently a phosphoryl guanidine linkage.

[00823] As widely known by those skilled in the art, natural phosphate linkages are widely found in natural DNA and RNA molecules; they have the structure of −OP(O)(OH)O−, connect sugars in the nucleosides in DNA and RNA, and may be in various salt forms, for example, at physiological pH (about 7.4), natural phosphate linkages are predominantly exist in salt forms with the anion being $-OP(O)(O^-)O-$. A modified internucleotidic linkage, or a non-natural phosphate linkage, is an internucleotidic linkage that is not natural phosphate linkage or a salt form thereof. Modified internucleotidic linkages, depending on their structures, may also be in their salt forms. For example, as appreciated by those skilled in the art, phosphorothioate internucleotidic linkages which have the structure of −OP(O)(SH)O− may be in various salt forms, e.g., at physiological pH (about 7.4) with the anion being $-OP(O)(S^-)O-$.

[00824] In some embodiments, an oligonucleotide comprises an internucleotidic linkage which is a modified internucleotidic linkage, e.g., phosphorothioate, phosphorodithioate, methylphosphonate, phosphoroamidate, thiophosphate, 3'-thiophosphate, or 5'-thiophosphate. In some embodiments, a modified internucleotidic linkage is a PN linkage. In some embodiments, a modified internucleotidic linkage is a PS linkage. In some embodiments, a modified internucleotidic linkage is a PO linkage (e.g., other than a natural phosphate linkage). In some embodiments, each modified internucleotidic linkage is independently a PN internucleotidic linkage or a PS internucleotidic linkage. In some embodiments, an oligonucleotide comprises one or more PN internucleotidic linkages, one or more PS internucleotidic linkages, and one or more PO internucleotidic linkages. In some embodiments, one or more PN internucleotidic linkages are independently phosphoramidate internucleotidic linkages. In some embodiments, one or more PN internucleotidic linkages are independently phosphoryl guanidine internucleotidic linkages. In some embodiments, one or more PN internucleotidic linkages are independently n001. In some embodiments, one or more PN internucleotidic linkages are independently n006. In some embodiments, one or more PN internucleotidic linkages are independently MsPA. In some embodiments, one or more PN internucleotidic linkages are independently n025. In some embodiments, each PN internucleotidic linkage is independently a phosphoramidate internucleotidic linkage. In some embodiments, each PN internucleotidic linkage independently is a phosphoryl guanidine internucleotidic linkage or MsPA. In some embodiments, each PN internucleotidic linkage is independently a

phosphoryl guanidine internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a n001 internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a n006 internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a n025 internucleotidic linkage. In some embodiments, a methylphosphonate internucleotidic linkage is utilized instead of a PN internucleotidic linkage at one or more positions. In some embodiments, one or more PS internucleotidic linkages are independently phosphorothioate internucleotidic linkages. In some embodiments, each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, one or more PO internucleotidic linkages are independently natural phosphate linkages. In some embodiments, each PO internucleotidic linkage is independently a natural phosphate linkage.

[00825] In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage which comprises a chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate linkage. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled with respect to its chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is stereochemically pure with respect to its chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is not chirally controlled. In some embodiments, a pattern of backbone chiral centers comprises or consists of positions and linkage phosphorus configurations of chirally controlled internucleotidic linkages (*R*p or *S*p) and positions of achiral internucleotidic linkages (e.g., natural phosphate linkages).

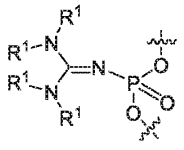
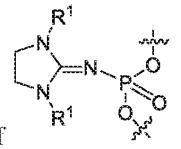
[00826] In some embodiments, an internucleotidic linkage comprises a P-modification, wherein a P-modification is a modification at a linkage phosphorus. In some embodiments, a modified internucleotidic linkage is a moiety which does not comprise a phosphorus but serves to link two sugars or two moieties that each independently comprises a nucleobase, e.g., as in peptide nucleic acid (PNA).

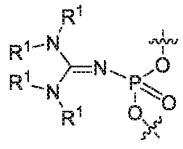
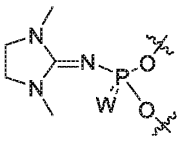
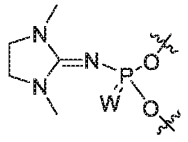
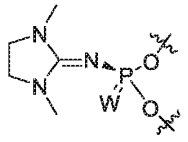
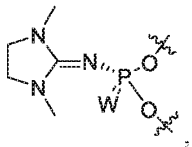
[00827] In some embodiments, an oligonucleotide comprises a modified internucleotidic linkage, e.g., those having the structure of Formula **I**, **I-a**, **I-b**, or **I-c** and described herein and/or in: WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the internucleotidic linkages (e.g., those of Formula **I**, **I-a**, **I-b**, **I-c**, etc.) of each of which are independently incorporated herein by reference. In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage.

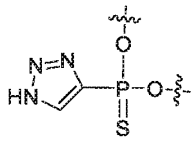
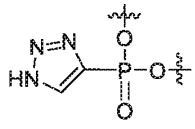
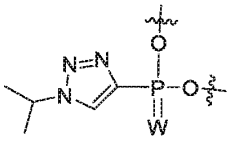
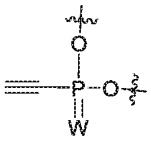
[00828] In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, provided oligonucleotides comprise one or more non-negatively charged internucleotidic linkages. In some embodiments, a non-negatively charged internucleotidic linkage is a positively charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, the present disclosure

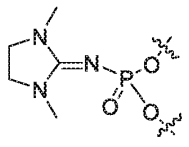
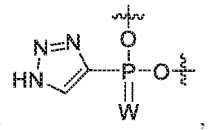
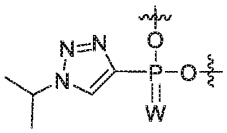
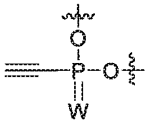
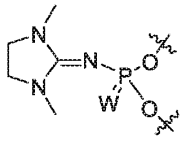
provides oligonucleotides comprising one or more neutral internucleotidic linkages. In some embodiments, a non-negatively charged internucleotidic linkage has the structure of Formula **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc., or a salt form thereof, as described herein and/or in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the non-negatively charged internucleotidic linkages (e.g., those of Formula **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc., or a suitable salt form thereof) of each of which are independently incorporated herein by reference.

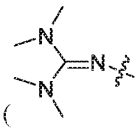
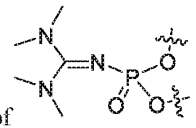
[00829] In some embodiments, a non-negatively charged internucleotidic linkage can improve the delivery and/or activities (e.g., adenosine editing activity).

[00830] In some embodiments, a modified internucleotidic linkage (e.g., a non-negatively charged internucleotidic linkage) comprises optionally substituted triazolyl. In some embodiments, a modified internucleotidic linkage (e.g., a non-negatively charged internucleotidic linkage) comprises optionally substituted alkynyl. In some embodiments, a modified internucleotidic linkage comprises a triazole or alkyne moiety. In some embodiments, a triazole moiety, e.g., a triazolyl group, is optionally substituted. In some embodiments, a triazole moiety, e.g., a triazolyl group) is substituted. In some embodiments, a triazole moiety is unsubstituted. In some embodiments, a modified internucleotidic linkage comprises an optionally substituted cyclic guanidine moiety. In some embodiments, a modified internucleotidic linkage, e.g., a phosphoryl guanidine internucleotidic linkage, has the structure of  and is optionally chirally controlled, wherein R^1 is –L–R', wherein L is L^B as described herein, and R' is as described herein. In some embodiments, each R^1 is independently R'. In some embodiments, each R' is independently R. In some embodiments, two R^1 are R and are taken together to form a ring as described herein. In some embodiments, two R^1 on two different nitrogen atoms are R and are taken together to form a ring as described herein. In some embodiments, R^1 is independently optionally substituted C_{1-6} aliphatic as described herein. In some embodiments, R^1 is methyl. In some embodiments, two R' on the same nitrogen atom are R and are taken together to form a ring as described herein. In some embodiments, a modified internucleotidic linkage, e.g., a phosphoryl guanidine internucleotidic linkage, has the structure of  and is optionally chirally

controlled. In some embodiments,  is . In some embodiments, a modified internucleotidic linkage, e.g., a phosphoryl guanidine internucleotidic linkage, comprises an optionally substituted cyclic guanidine moiety and has the structure of: , , or , wherein W is O or S. In some embodiments, W is O. In some embodiments, W is S. In some embodiments, a non-negatively charged internucleotidic linkage is stereochemically controlled.

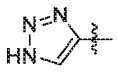
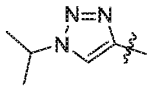
[00831] In some embodiments, a non-negatively charged internucleotidic linkage or a neutral internucleotidic linkage is an internucleotidic linkage comprising a triazole moiety. In some embodiments, a non-negatively charged internucleotidic linkage or a non-negatively charged internucleotidic linkage comprises an optionally substituted triazolyl group. In some embodiments, an internucleotidic linkage comprising a triazole moiety (e.g., an optionally substituted triazolyl group) has the structure of . In some embodiments, an internucleotidic linkage comprising a triazole moiety has the structure of . In some embodiments, an internucleotidic linkage comprising a triazole moiety has the formula of , where W is O or S. In some embodiments, an internucleotidic linkage comprising an alkyne moiety (e.g., an optionally substituted alkynyl group) has the formula of , wherein W is O or S. In some embodiments, an internucleotidic linkage, e.g., a non-negatively charged internucleotidic linkage, a neutral internucleotidic linkage, comprises a cyclic guanidine moiety. In some embodiments, an internucleotidic linkage comprising a cyclic guanidine moiety

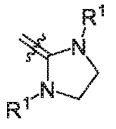
has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage, or a neutral internucleotidic linkage, is or comprising a structure selected from , , , or , wherein W is O or S.

[00832] In some embodiments, an internucleotidic linkage comprises a Tmg group (). In some embodiments, an internucleotidic linkage comprises a Tmg group and has the structure of  (the "Tmg internucleotidic linkage"). In some embodiments, neutral internucleotidic linkages include internucleotidic linkages of PNA and PMO, and an Tmg internucleotidic linkage.

[00833] In some embodiments, a non-negatively charged internucleotidic linkage has the structure of Formula **I**, **I-a**, **I-b**, **I-c**, **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc., or a salt form thereof. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 3-20 membered heterocyclyl or heteroaryl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 3-20 membered heterocyclyl or heteroaryl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, such a heterocyclyl or heteroaryl group is of a 5-membered ring. In some embodiments, such a heterocyclyl or heteroaryl group is of a 6-membered ring.

[00834] In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heteroaryl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heteroaryl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-6 membered heteroaryl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-membered heteroaryl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a heteroaryl group

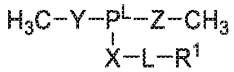
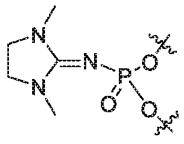
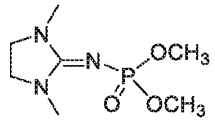
is directly bonded to a linkage phosphorus. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted triazolyl group. In some embodiments, a non-negatively charged internucleotidic linkage comprises an unsubstituted triazolyl group, e.g., . In some embodiments, a non-negatively charged internucleotidic linkage comprises a substituted triazolyl group, e.g., .

[00835] In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heterocyclyl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heterocyclyl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-6 membered heterocyclyl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-membered heterocyclyl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, at least two heteroatoms are nitrogen. In some embodiments, a heterocyclyl group is directly bonded to a linkage phosphorus. In some embodiments, a heterocyclyl group is bonded to a linkage phosphorus through a linker, e.g., =N– when the heterocyclyl group is part of a guanidine moiety who directed bonded to a linkage phosphorus through its =N–. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted  group. In some embodiments, a non-negatively charged internucleotidic linkage comprises an substituted  group. In some embodiments, a non-negatively charged internucleotidic linkage comprises a  group, wherein each R^1 is independently –L–R. In some embodiments, each R^1 is independently optionally substituted C_{1-6} alkyl. In some embodiments, each R^1 is independently methyl.

[00836] In some embodiments, a modified internucleotidic linkage, e.g., a non-negatively charged internucleotidic linkage, comprises a triazole or alkyne moiety, each of which is optionally substituted. In some embodiments, a modified internucleotidic linkage comprises a triazole moiety. In some embodiments, a modified internucleotidic linkage comprises a unsubstituted triazole moiety. In some embodiments, a modified internucleotidic linkage comprises a substituted triazole moiety. In some embodiments, a modified

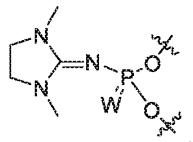
internucleotidic linkage comprises an alkyl moiety. In some embodiments, a modified internucleotidic linkage comprises an optionally substituted alkynyl group. In some embodiments, a modified internucleotidic linkage comprises an unsubstituted alkynyl group. In some embodiments, a modified internucleotidic linkage comprises a substituted alkynyl group. In some embodiments, an alkynyl group is directly bonded to a linkage phosphorus.

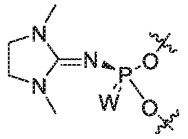
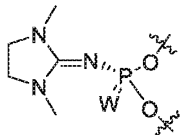
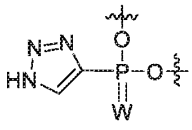
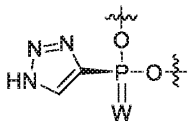
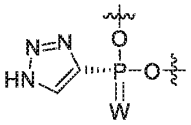
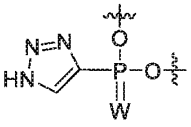
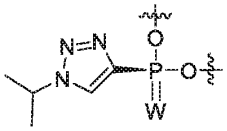
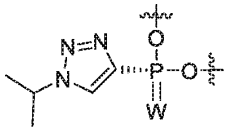
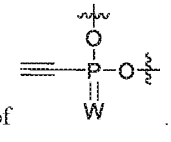
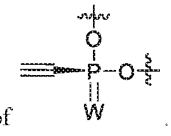
[00837] In some embodiments, an oligonucleotide comprises different types of internucleotidic phosphorus linkages. In some embodiments, a chirally controlled oligonucleotide comprises at least one natural phosphate linkage and at least one modified (non-natural) internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least one natural phosphate linkage and at least one phosphorothioate. In some embodiments, an oligonucleotide comprises at least one non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least one natural phosphate linkage and at least one non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least one phosphorothioate internucleotidic linkage and at least one non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least one phosphorothioate internucleotidic linkage, at least one natural phosphate linkage, and at least one non-negatively charged internucleotidic linkage. In some embodiments, oligonucleotides comprise one or more, e.g., 1-50, 1-40, 1-30, 1-20, 1-15, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more non-negatively charged internucleotidic linkages. In some embodiments, oligonucleotides comprise no more than a certain number of non-negatively charged internucleotidic linkages, e.g., no more than 1, no more than 2, no more than 3, no more than 4, no more than 5, no more than 6, no more than 7, no more than 8, no more than 9, no more than 10, no more than 11, no more than 12, no more than 13, no more than 14, no more than 15, no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, no more than 22, no more than 23, no more than 24, no more than 25, no more than 26, no more than 27, no more than 28, no more than 29, or no more than 30 non-negatively charged internucleotidic linkages. In some embodiments, oligonucleotides comprise no non-negatively charged internucleotidic linkages. In some embodiments, a non-negatively charged internucleotidic linkage is not negatively charged in that at a given pH in an aqueous solution less than 50%, 40%, 40%, 30%, 20%, 10%, 5%, or 1% of the internucleotidic linkage exists in a negatively charged salt form. In some embodiments, a pH is about pH 7.4. In some embodiments, a pH is about 4-9. In some embodiments, the percentage is less than 10%. In some embodiments, the percentage is less than 5%. In some embodiments, the percentage is less than 1%. In some embodiments, an internucleotidic linkage is a non-negatively charged internucleotidic linkage in that the neutral form of the internucleotidic linkage has no pKa that is no more than about 1, 2, 3, 4, 5, 6, or 7 in water. In some embodiments, no pKa is 7 or less. In some embodiments, no pKa is 6 or less. In some embodiments, no pKa is 5 or less. In some embodiments, no pKa is 4 or less. In some embodiments, no pKa is 3 or less. In some embodiments, no pKa is 2 or less. In some embodiments, no pKa is 1 or less. In some embodiments, pKa of the neutral form of an internucleotidic linkage can be represented by pKa of the neutral form of a compound

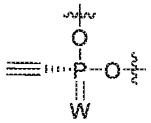
having the structure of CH_3–the internucleotidic linkage–CH_3. For example, pKa of the neutral form of an internucleotidic linkage having the structure of Formula I may be represented by the pKa of the neutral form of a compound having the structure of  (wherein each of X, Y, Z is independently –O–, –S–, –N(R')–; L is L^B, and R^1 is –L–R'), pKa of  can be represented by pKa . In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a positively-charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage comprises a guanidine moiety. In some embodiments, a non-negatively charged internucleotidic linkage comprises a heteroaryl base moiety. In some embodiments, a non-negatively charged internucleotidic linkage comprises a triazole moiety. In some embodiments, a non-negatively charged internucleotidic linkage comprises an alkynyl moiety.

[00838] In some embodiments, a neutral or non-negatively charged internucleotidic linkage has the structure of any neutral or non-negatively charged internucleotidic linkage described in any of: US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, each neutral or non-negatively charged internucleotidic linkage of each of which is hereby incorporated by reference.

[00839] In some embodiments, each R' is independently optionally substituted C_{1-6} aliphatic. In some embodiments, each R' is independently optionally substituted C_{1-6} alkyl. In some embodiments, each R' is independently $-CH_3$. In some embodiments, each R^s is –H.

[00840] In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure

of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage has the structure of . In some embodiments,

a non-negatively charged internucleotidic linkage has the structure of . In some embodiments, W is O. In some embodiments, W is S. In some embodiments, a neutral internucleotidic linkage is a non-negatively charged internucleotidic linkage described above.

[00841] In some embodiments, provided oligonucleotides comprise 1 or more internucleotidic linkages of Formula **I, I-a, I-b, I-c, I-n-1, I-n-2, I-n-3, I-n-4, II, II-a-1, II-a-2, II-b-1, II-b-2, II-c-1, II-c-2, II-d-1,** or **II-d-2**, which are described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the Formula **I, I-a, I-b, I-c, I-n-1, I-n-2, I-n-3, I-n-4, II, II-a-1, II-a-2, II-b-1, II-b-2, II-c-1, II-c-2, II-d-1,** or **II-d-2**, or salt forms thereof of each of which are independently incorporated herein by reference.

[00842] In some embodiments, an oligonucleotide comprises a neutral internucleotidic linkage and a chirally controlled internucleotidic linkage. In some embodiments, an oligonucleotide comprises a neutral internucleotidic linkage and a chirally controlled internucleotidic linkage which is not the neutral internucleotidic linkage. In some embodiments, an oligonucleotide comprises a neutral internucleotidic linkage and a chirally controlled phosphorothioate internucleotidic linkage. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more non-negatively charged internucleotidic linkages and one or more phosphorothioate internucleotidic linkages, wherein each phosphorothioate internucleotidic linkage in the oligonucleotide is independently a chirally controlled internucleotidic linkage. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more neutral internucleotidic linkages and one or more phosphorothioate internucleotidic linkage, wherein each phosphorothioate internucleotidic linkage in the oligonucleotide is independently a chirally controlled internucleotidic linkage. In some embodiments, an oligonucleotide comprises at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more chirally controlled phosphorothioate internucleotidic linkages. In some embodiments, non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a neutral internucleotidic linkage is chirally controlled. In some embodiments, a neutral internucleotidic linkage is not chirally controlled. In some embodiments, an oligonucleotide comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) chirally controlled and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled chiral internucleotidic linkages. In some embodiments, an oligonucleotide comprises one or more (e.g., 1, 2, 3, 4, 5,

6, 7, 8, 9, or 10) chirally controlled and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled non-negatively charged internucleotidic linkages (in some embodiments, each of which is independently n001). In some embodiments, a neutral internucleotidic linkage is chirally controlled. In some embodiments, a neutral internucleotidic linkage is not chirally controlled. In some embodiments, an oligonucleotide comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) chirally controlled and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) non-chirally controlled neutral internucleotidic linkages (in some embodiments, each of which is independently n001).

[00843] Without wishing to be bound by any particular theory, the present disclosure notes that a neutral internucleotidic linkage can be more hydrophobic than a negatively charged internucleotidic linkage, e.g., a phosphorothioate internucleotidic linkage, which can be more hydrophobic than a natural phosphate linkage. Typically, unlike a phosphorothioate internucleotidic linkage or natural phosphate linkage, a neutral internucleotidic linkage bears less charge. Without wishing to be bound by any particular theory, the present disclosure notes that incorporation of one or more neutral internucleotidic linkages into an oligonucleotide may increase oligonucleotides' ability to be taken up by a cell and/or to escape from endosomes. Without wishing to be bound by any particular theory, the present disclosure notes that incorporation of one or more neutral internucleotidic linkages can be utilized to modulate melting temperature of duplexes formed between an oligonucleotide and its target nucleic acid.

[00844] Without wishing to be bound by any particular theory, the present disclosure notes that incorporation of one or more non-negatively charged internucleotidic linkages, e.g., neutral internucleotidic linkages, into an oligonucleotide may be able to increase the oligonucleotide's ability to mediate a function such as target adenosine editing.

[00845] As appreciated by those skilled in the art, internucleotidic linkages such as natural phosphate linkages and those of Formula **I**, **I-a**, **I-b**, **I-c**, **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, or salt forms thereof typically connect two nucleosides (which can either be natural or modified) as described in US 9394333, US 9744183, US 9605019, US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the Formula **I**, **I-a**, **I-b**, **I-c**, **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, or salt forms thereof of each of which are independently incorporated herein by reference. A typical connection, as in natural DNA and RNA, is that an internucleotidic linkage forms bonds with two sugars (which can be either unmodified or modified as described herein). In many embodiments, as exemplified herein, an internucleotidic linkage forms bonds through oxygen atoms or heteroatoms (e.g., Y and Z in various formulae) with one optionally modified ribose or deoxyribose at its 5' carbon, and the other optionally modified ribose or deoxyribose at its 3' carbon. In some embodiments, each

nucleoside units connected by an internucleotidic linkage independently comprises a nucleobase which is independently an optionally substituted A, T, C, G, or U, or a substituted tautomer of A, T, C, G or U, or a nucleobase comprising an optionally substituted heterocyclyl and/or a heteroaryl ring having at least one nitrogen atom.

[00846] In some embodiments, a linkage has the structure of or comprises $-Y-P^L(-X-R^L)-Z-$, or a salt form thereof, wherein:

P^L is P, P(=W), P-->B(--L^L--R^L)$_3$, or P^N;

W is O, N(–L^L–R^L), S or Se;

P^N is P=N–C(–L^L–R')(=L^N–R') or P=N–L^L–R^L;

L^N is =N--L^{LI}--, =CH--L^{LI}-- wherein CH is optionally substituted, or =N^+(R')(Q^-)--L^{LI}--;

Q^- is an anion;

each of X, Y and Z is independently –O–, –S–, --L^L--N(--L^L--R^L)--L^L--, --L^L--N=C(--L^L--R^L)--L^L--, or L^L;

each R^L is independently $-L^L$–N(R')$_2$, –L^L–R', –N=C(–L^L–R')$_2$, –L^L–N(R')C(NR')N(R')$_2$, –L^L–N(R')C(O)N(R')$_2$, a carbohydrate, or one or more additional chemical moieties optionally connected through a linker;

each of L^{LI} and L^L is independently L;

$-Cy^{IL}-$ is –Cy–;

each L is independently a covalent bond, or a bivalent, optionally substituted, linear or branched group selected from a C_{1-30} aliphatic group and a C_{1-30} heteroaliphatic group having 1-10 heteroatoms, wherein one or more methylene units are optionally and independently replaced by an optionally substituted group selected from C_{1-6} alkylene, C_{1-6} alkenylene, —C≡C—, a bivalent C_1–C_6 heteroaliphatic group having 1-5 heteroatoms, –C(R')$_2$–, –Cy–, –O–, –S–, –S–S–, –N(R')–, –C(O)–, –C(S)–, –C(NR')–, –C(NR')N(R')–, –N(R')C(NR')N(R')–, –C(O)N(R')–, –N(R')C(O)N(R')–, –N(R')C(O)O–, –S(O)–, –S(O)$_2$–, –S(O)$_2$N(R')–, –C(O)S–, –C(O)O–, –P(O)(OR')–, –P(O)(SR')–, –P(O)(R')–, –P(O)(NR')–, –P(S)(OR')–, –P(S)(SR')–, –P(S)(R')–, –P(S)(NR')–, –P(R')–, –P(OR')–, –P(SR')–, –P(NR')–, –P(OR')[B(R')$_3$]–, –OP(O)(OR')O–, –OP(O)(SR')O–, –OP(O)(R')O–, –OP(O)(NR')O–, –OP(OR')O–, –OP(SR')O–, –OP(NR')O–, –OP(R')O–, –OP(OR')[B(R')$_3$]O–, and –[C(R')$_2$C(R')$_2$O]n–, wherein n is 1-50, and one or more nitrogen or carbon atoms are optionally and independently replaced with Cy^L;

each –Cy– is independently an optionally substituted bivalent 3-30 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms;

each Cy^L is independently an optionally substituted trivalent or tetravalent, 3-30 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms;

each R' is independently –R, –C(O)R, –C(O)N(R)$_2$, –C(O)OR, or –S(O)$_2$R;

each R is independently –H, or an optionally substituted group selected from C_{1-30} aliphatic, C_{1-30}

heteroaliphatic having 1-10 heteroatoms, C_{6-30} aryl, C_{6-30} arylaliphatic, C_{6-30} arylheteroaliphatic having 1-10 heteroatoms, 5-30 membered heteroaryl having 1-10 heteroatoms, and 3-30 membered heterocyclyl having 1-10 heteroatoms, or

two R groups are optionally and independently taken together to form a covalent bond, or:

two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms; or

two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms.

[00847] In some embodiments, an internucleotidic linkage has the structure of $-O-P^L(-X-R^L)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)(-X-R^L)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)[-N(-L^L-R^L)-R^L]-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)(-NH-L^L-R^L)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)[-N(R')_2]-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)(-NHR')-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)(-NHSO_2R)-O-$, wherein each variable is independently as described herein. In some embodiments, R is methyl. In some embodiments, an internucleotidic linkage is $-O-P(=O)(-NHSO_2CH_3)-O-$. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)[-N=C(-L^L-R')_2]-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-O-P(=W)[-N=C[N(R')_2]_2]-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-OP(=W)(-N=C(R'')_2)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-OP(=W)(-N(R'')_2)-O-$, wherein each variable is independently as described herein. In some embodiments, W is O. In some embodiments, W is S. In some embodiments, such an internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, such an internucleotidic linkage is a neutral internucleotidic linkage.

[00848] In some embodiments, an internucleotidic linkage has the structure of $-P^L(-X-R^L)-Z-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-P^L(-X-R^L)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of $-P(=W)(-X-R^L)-O-$, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of

–P(=W)[–N(–L^L–R^L)–R^L]–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)(–NH–L^L–R^L)–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)[–N(R')$_2$]–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)(–NHR')–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)(–NHSO$_2$R)–O–, wherein each variable is independently as described herein. In some embodiments, R is methyl. In some embodiments, an internucleotidic linkage is –P(=O)(–NHSO$_2$CH$_3$)–O–. In some embodiments, an internucleotidic linkage has the structure of –P(=W)[–N=C(–L^L–R')$_2$]–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)[–N=C[N(R')$_2$]$_2$]–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)(–N=C(R")$_2$)–O–, wherein each variable is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=W)(–N(R")$_2$)–O–, wherein each variable is independently as described herein. In some embodiments, W is O. In some embodiments, W is S. In some embodiments, such an internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, such an internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, P of such an internucleotidic linkage is bonded to N of a sugar.

[00849] In some embodiments, a linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a linkage is a thio-phosphoryl guanidine internucleotidic linkage.

[00850] In some embodiments, one or more methylene units are optionally and independently replaced with a moiety as described herein. In some embodiments, L or L^L is or comprises –SO$_2$–. In some embodiments, L or L^L is or comprises –SO$_2$N(R')–. In some embodiments, L or L^L is or comprises –C(O)–. In some embodiments, L or L^L is or comprises –C(O)O–. In some embodiments, L or L^L is or comprises –C(O)N(R')–. In some embodiments, L or L^L is or comprises –P(=W)(R')–. In some embodiments, L or L^L is or comprises –P(=O)(R')–. In some embodiments, L or L^L is or comprises –P(=S)(R')–. In some embodiments, L or L^L is or comprises –P(R')–. In some embodiments, L or L^L is or comprises –P(=W)(OR')–. In some embodiments, L or L^L is or comprises –P(=O)(OR')–. In some embodiments, L or L^L is or comprises –P(=S)(OR')–. In some embodiments, L or L^L is or comprises –P(OR')–.

[00851] In some embodiments, –X–R^L is –N(R')SO$_2$$R^L$. In some embodiments, –X–R^L is –N(R')C(O)R^L. In some embodiments, –X–R^L is –N(R')P(=O)(R')R^L.

[00852] In some embodiments, a linkage, e.g., a non-negatively charged internucleotidic linkage or neutral internucleotidic linkage, has the structure of or comprises –P(=W)(–N=C(R")$_2$)–, –P(=W)(–N(R')SO$_2$R")–, –P(=W)(–N(R')C(O)R")–, –P(=W)(–N(R")$_2$)–, –P(=W)(–N(R')P(O)(R")$_2$)–, –OP(=W)(–N=C(R")$_2$)O–, –OP(=W)(–N(R')SO$_2$R")O–, –OP(=W)(–N(R')C(O)R")O–, –OP(=W)(–N(R")$_2$)O–, –OP(=W)(–N(R')P(O)(R")$_2$)O–, –P(=W)(–N=C(R")$_2$)O–, –P(=W)(–N(R')SO$_2$R")O–,

–P(=W)(–N(R')C(O)R")O–, –P(=W)(–N(R")$_2$)O–, or –P(=W)(–N(R')P(O)(R")$_2$)O–, or a salt form thereof, wherein:

W is O or S;

each R" is independently R', –OR', –P(=W)(R')$_2$, or –N(R')$_2$;

each R' is independently –R, –C(O)R, –C(O)N(R)$_2$, –C(O)OR, or –S(O)$_2$R;

each R is independently –H, or an optionally substituted group selected from C$_{1-30}$ aliphatic, C$_{1-30}$ heteroaliphatic having 1-10 heteroatoms, C$_{6-30}$ aryl, C$_{6-30}$ arylaliphatic, C$_{6-30}$ arylheteroaliphatic having 1-10 heteroatoms, 5-30 membered heteroaryl having 1-10 heteroatoms, and 3-30 membered heterocyclyl having 1-10 heteroatoms, or

two R groups are optionally and independently taken together to form a covalent bond, or:

two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms; or

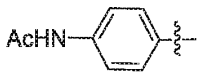
two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms.

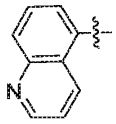
[00853] In some embodiments, W is O. In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–N=C(R")$_2$)–, –P(=O)(–N(R')SO$_2$R")–, –P(=O)(–N(R')C(O)R")–, –P(=O)(–N(R")$_2$)–, –P(=O)(–N(R')P(O)(R")$_2$)–, –OP(=O)(–N=C(R")$_2$)O–, –OP(=O)(–N(R')SO$_2$R")O–, –OP(=O)(–N(R')C(O)R")O–, –OP(=O)(–N(R")$_2$)O–, –OP(=O)(–N(R')P(O)(R")$_2$)O–, –P(=O)(–N=C(R")$_2$)O–, –P(=O)(–N(R')SO$_2$R")O–, –P(=O)(–N(R')C(O)R")O–, –P(=O)(–N(R")$_2$)O–, or –P(=O)(–N(R')P(O)(R")$_2$)O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–N=C(R")$_2$)– –P(=O)(–N(R")$_2$)–, –OP(=O)(–N=C(R")$_2$)–O–, –OP(=O)(–N(R")$_2$)–O–, –P(=O)(–N=C(R")$_2$)–O– or –P(=O)(–N(R")$_2$)–O– or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N=C(R")$_2$)–O– or –OP(=O)(–N(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N=C(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N(R')SO$_2$R")O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N(R')C(O)R")O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N(R')P(O)(R")$_2$)O–, or a salt form thereof. In some embodiments, a internucleotidic linkage is n001.

[00854] In some embodiments, W is S. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–N=C(R")$_2$)–, –P(=S)(–N(R')SO$_2$R")–, –P(=S)(–N(R')C(O)R")–, –P(=S)(–N(R")$_2$)–, –P(=S)(–N(R')P(O)(R")$_2$)–, –OP(=S)(–N=C(R")$_2$)O–, –OP(=S)(–N(R')SO$_2$R")O–,

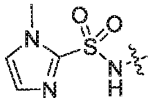
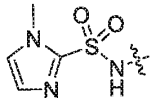
–OP(=S)(–N(R')C(O)R")O–, –OP(=S)(–N(R")$_2$)O–, –OP(=S)(–N(R')P(O)(R")$_2$)O–, –P(=S)(–N=C(R")$_2$)O–, –P(=S)(–N(R')SO_2R")O–, –P(=S)(–N(R')C(O)R")O–, –P(=S)(–N(R")$_2$)O–, or –P(=S)(–N(R')P(O)(R")$_2$)O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–N=C(R")$_2$)– –P(=S)(–N(R")$_2$)–, –OP(=S)(–N=C(R")$_2$)–O–, –OP(=S)(–N(R")$_2$)–O–, –P(=S)(–N=C(R")$_2$)–O– or –P(=S)(–N(R")$_2$)–O– or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N=C(R")$_2$)–O– or –OP(=S)(–N(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N=C(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N(R")$_2$)–O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N(R')SO_2R")O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N(R')C(O)R")O–, or a salt form thereof. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N(R')P(O)(R")$_2$)O–, or a salt form thereof. In some embodiments, a internucleotidic linkage is *n001.

[00855] In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–N(R')SO_2R")–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–N(R')SO_2R")–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–N(R')SO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–N(R')SO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–N(R')SO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–N(R')SO_2R")O–, wherein R" is as described herein. In some embodiments, R', e.g., of –N(R')–, is hydrogen or optionally substituted C_{1-6} aliphatic. In some embodiments, R' is C_{1-6} alkyl. In some embodiments, R' is hydrogen. In some embodiments, R", e.g., in –SO_2R", is R' as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–NHSO_2R")–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–NHSO_2R")–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=O)(–NHSO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –P(=S)(–NHSO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –OP(=O)(–NHSO_2R")O–, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of –OP(=S)(–NHSO_2R")O–, wherein R" is as described herein. In some embodiments, –X–R^L is –N(R')SO_2R^L, wherein each of R' and R^L is independently as described herein. In some embodiments, R^L is R". In some embodiments, R^L is R'. In some embodiments, –X–R^L is –N(R')SO_2R", wherein R' is as described herein. In some embodiments, –X–R^L is –N(R')SO_2R', wherein R' is as described herein. In some embodiments, –X–R^L is –NHSO_2R', wherein R' is as described herein. In some embodiments, R' is R as described herein. In some embodiments, R' is optionally substituted C_{1-6} aliphatic. In some embodiments, R' is optionally substituted C_{1-6} alkyl. In some embodiments,

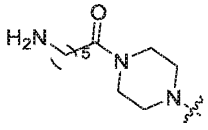
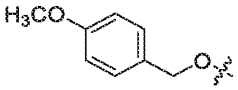
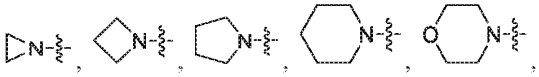
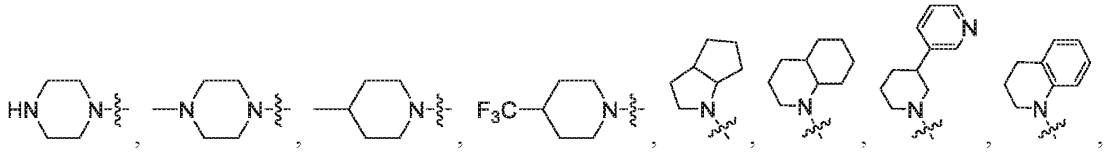
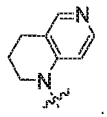
R' is optionally substituted phenyl. In some embodiments, R' is optionally substituted heteroaryl. In some embodiments, R", e.g., in $-SO_2R"$, is R. In some embodiments, R is an optionally substituted group selected from C_{1-6} aliphatic, aryl, heterocyclyl, and heteroaryl. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted C_{1-6} alkenyl. In some embodiments, R is optionally substituted C_{1-6} alkynyl. In some embodiments, R is optionally substituted methyl. In some embodiments, $-X-R^L$ is $-NHSO_2CH_3$. In some embodiments, R is $-CF_3$. In some embodiments, R is methyl. In some embodiments, R is optionally substituted ethyl. In some embodiments, R is ethyl. In some embodiments, R is $-CH_2CHF_2$. In some embodiments, R is $-CH_2CH_2OCH_3$. In some embodiments, R is optionally substituted propyl. In some embodiments, R is optionally substituted butyl. In some embodiments, R is n-butyl. In some embodiments, R is $-(CH_2)_6NH_2$. In some embodiments, R is an optionally substituted linear C_{2-20} aliphatic. In some embodiments, R is optionally substituted linear C_{2-20} alkyl. In some embodiments, R is linear C_{2-20} alkyl. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} aliphatic. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is optionally substituted linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl. In some embodiments, R is p-methylphenyl. In some embodiments, R is 4-dimethylaminophenyl. In some embodiments, R is 3-pyridinyl. In some embodiments, R is 

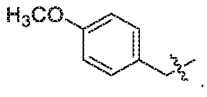
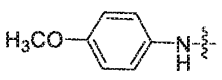
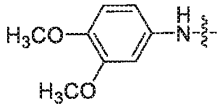
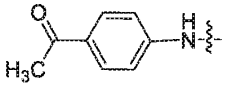
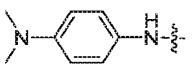
. In some embodiments, R is 

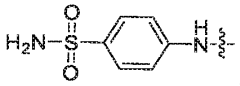
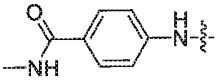
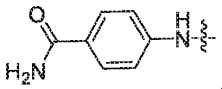
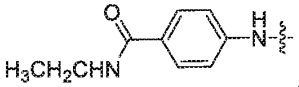
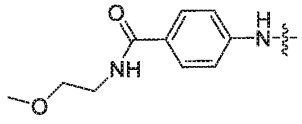
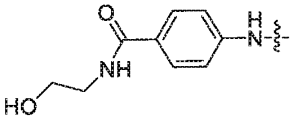
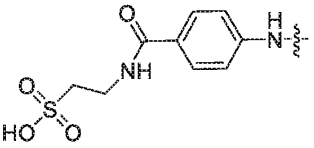
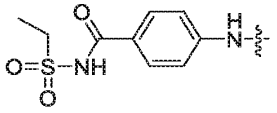
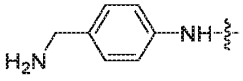
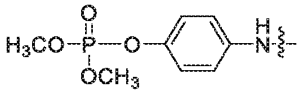
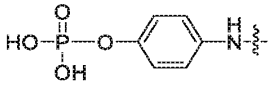
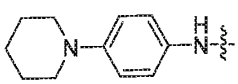
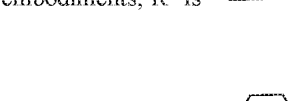
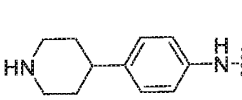
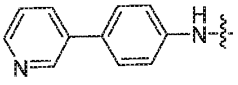
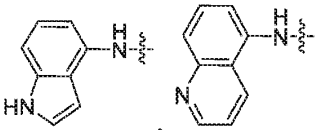
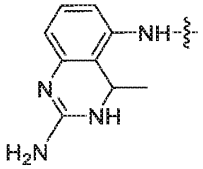
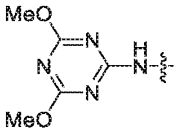
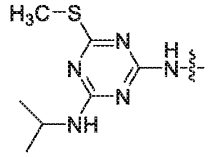
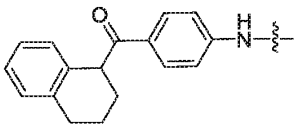
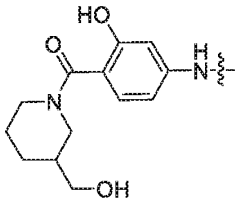
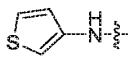
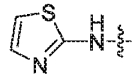
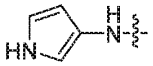
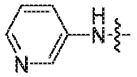
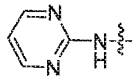
. In some embodiments, R is benzyl. In some embodiments, R is optionally substituted heteroaryl. In some embodiments, R is optionally substituted 1,3-diazolyl. In some embodiments, R is optionally substituted 2-(1,3)-diazolyl. In some embodiments, R is optionally substituted 1-methyl-2-(1,3)-diazolyl. In some embodiments, R is isopropyl. In some embodiments, R" is $-N(R')_2$. In some embodiments, R" is $-N(CH_3)_2$. In some embodiments, R", e.g., in $-SO_2R"$, is $-OR'$, wherein R' is as described herein. In some embodiments, R' is R as described herein. In some embodiments, R" is $-OCH_3$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2R)O-$, wherein R is as described herein. In some embodiments, R is optionally substituted linear alkyl as described herein. In some embodiments, R is linear alkyl as described herein. In some embodiments, a linkage is $-OP(=O)(-NHSO_2CH_3)O-$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2CH_2CH_3)O-$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2CH_2CH_2OCH_3)O-$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2CH_2Ph)O-$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2CH_2CHF_2)O-$. In some embodiments, a linkage is $-OP(=O)(-NHSO_2(4\text{-methylphenyl}))O-$. In some embodiments, $-X-R^L$ is

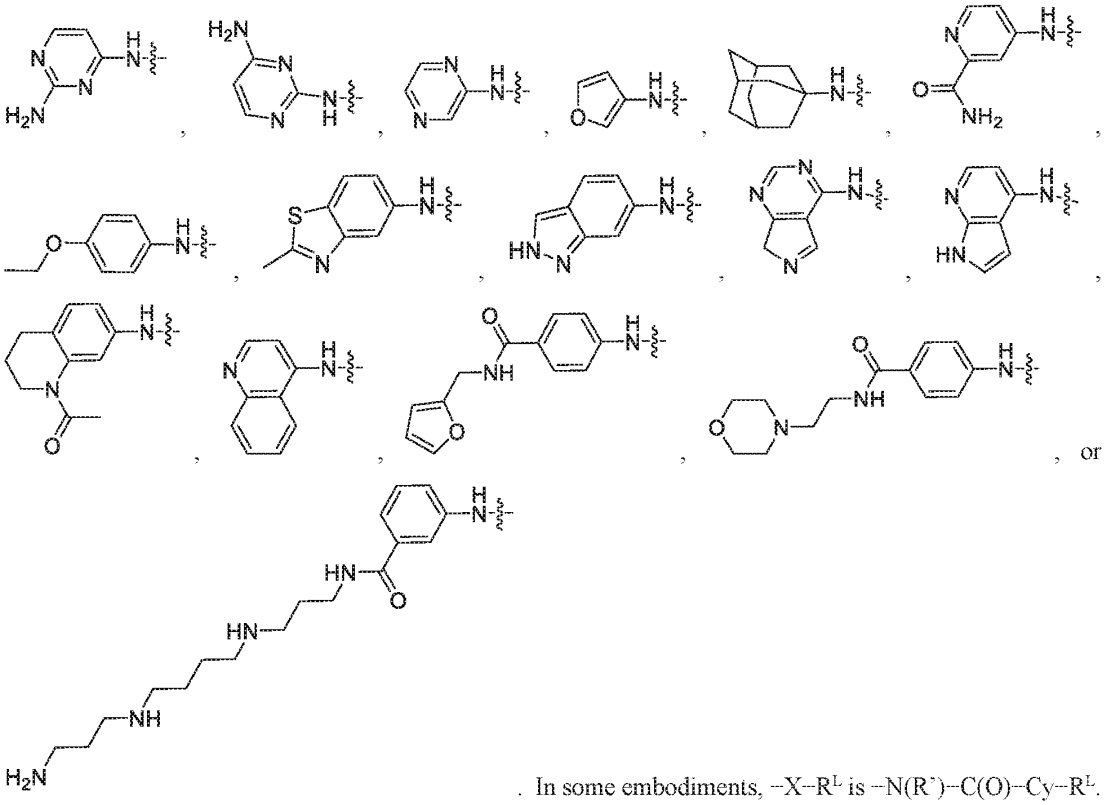
. In some embodiments, a linkage is −OP(=O)(−X−R^L)O−, wherein −X−R^L is . In some embodiments, a linkage is −OP(=O)(−$NHSO_2CH(CH_3)_2$)O−. In some embodiments, a linkage is −OP(=O)(−$NHSO_2N(CH_3)_2$)O−. In some embodiments, a linkage is n002. In some embodiments, a linkage is n006. In some embodiments, a linkage is n020. In some embodiments, such internucleotidic linkages may be utilized in place of linkages like n001.

[00856] In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−N(R')C(O)R")−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−N(R')C(O)R")−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−N(R')C(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−N(R')C(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=O)(−N(R')C(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=S)(−N(R')C(O)R")O−, wherein R" is as described herein. In some embodiments, R', e.g., of −N(R')−, is hydrogen or optionally substituted C_{1-6} aliphatic. In some embodiments, R' is C_{1-6} alkyl. In some embodiments, R' is hydrogen. In some embodiments, R", e.g., in −C(O)R", is R' as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−NHC(O)R")−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−NHC(O)R")−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−NHC(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−NHC(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=O)(−NHC(O)R")O−, wherein R" is as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=S)(−NHC(O)R")O−, wherein R" is as described herein. In some embodiments, −X−R^L is −N(R')COR^L−, wherein R^L is as described herein. In some embodiments, −X−R^L is −N(R')COR", wherein R" is as described herein. In some embodiments, −X−R^L is −N(R')COR', wherein R' is as described herein. In some embodiments, −X−R^L is −NHCOR', wherein R' is as described herein. In some embodiments, R' is R as described herein. In some embodiments, R' is optionally substituted C_{1-6} aliphatic. In some embodiments, R' is optionally substituted C_{1-6} alkyl. In some embodiments, R' is optionally substituted phenyl. In some embodiments, R' is optionally substituted heteroaryl. In some embodiments, R", e.g., in −C(O)R", is R. In some embodiments, R is an optionally substituted group selected from C_{1-6} aliphatic, aryl, heterocyclyl, and heteroaryl. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted C_{1-6} alkenyl. In some embodiments, R is optionally substituted C_{1-6} alkynyl. In some embodiments, R is methyl. In some embodiments, −X−R^L is −$NHC(O)CH_3$. In some embodiments, R is optionally substituted methyl.

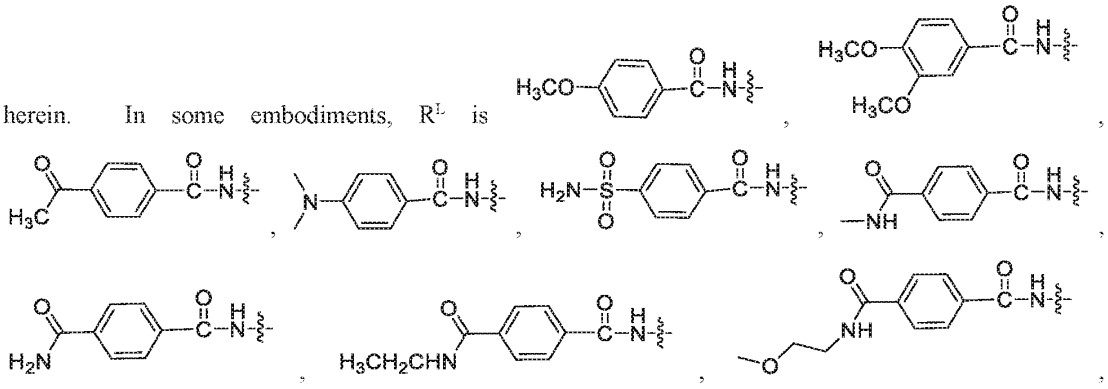
In some embodiments, R is $-CF_3$. In some embodiments, R is optionally substituted ethyl. In some embodiments, R is ethyl. In some embodiments, R is $-CH_2CHF_2$. In some embodiments, R is $-CH_2CH_2OCH_3$. In some embodiments, R is optionally substituted C_{1-20} (e.g., C_{1-6}, C_{2-6}, C_{3-6}, C_{1-10}, C_{2-10}, C_{3-10}, C_{2-20}, C_{3-20}, C_{10-20}, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) aliphatic. In some embodiments, R is optionally substituted C_{1-20} (e.g., C_{1-6}, C_{2-6}, C_{3-6}, C_{1-10}, C_{2-10}, C_{3-10}, C_{2-20}, C_{3-20}, C_{10-20}, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) alkyl. In some embodiments, R is an optionally substituted linear C_{2-20} aliphatic. In some embodiments, R is optionally substituted linear C_{2-20} alkyl. In some embodiments, R is linear C_{2-20} alkyl. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} aliphatic. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is optionally substituted linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is optionally substituted aryl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is p-methylphenyl. In some embodiments, R is benzyl. In some embodiments, R is optionally substituted heteroaryl. In some embodiments, R is optionally substituted 1,3-diazolyl. In some embodiments, R is optionally substituted 2-(1,3)-diazolyl. In some embodiments, R is optionally substituted 1-methyl-2-(1,3)-diazolyl. In some embodiments, R^L is $-(CH_2)_5NH_2$. In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R" is $-N(R')_2$. In some embodiments, R" is $-N(CH_3)_2$. In some embodiments, $-X-R^L$ is $-N(R')CON(R^L)_2$, wherein each of R' and R^L is independently as described herein. In some embodiments, $-X-R^L$ is $-NHCON(R^L)_2$, wherein R^L is as described herein. In some embodiments, two R' or two R^L are taken together with the nitrogen atom to which they are attached to form a ring as described herein, e.g., optionally substituted , , or . In some embodiments, R", e.g., in $-C(O)R"$, is $-OR'$, wherein R' is as described herein. In some embodiments, R' is R as described herein. In some embodiments, is optionally substituted C_{1-6} aliphatic.

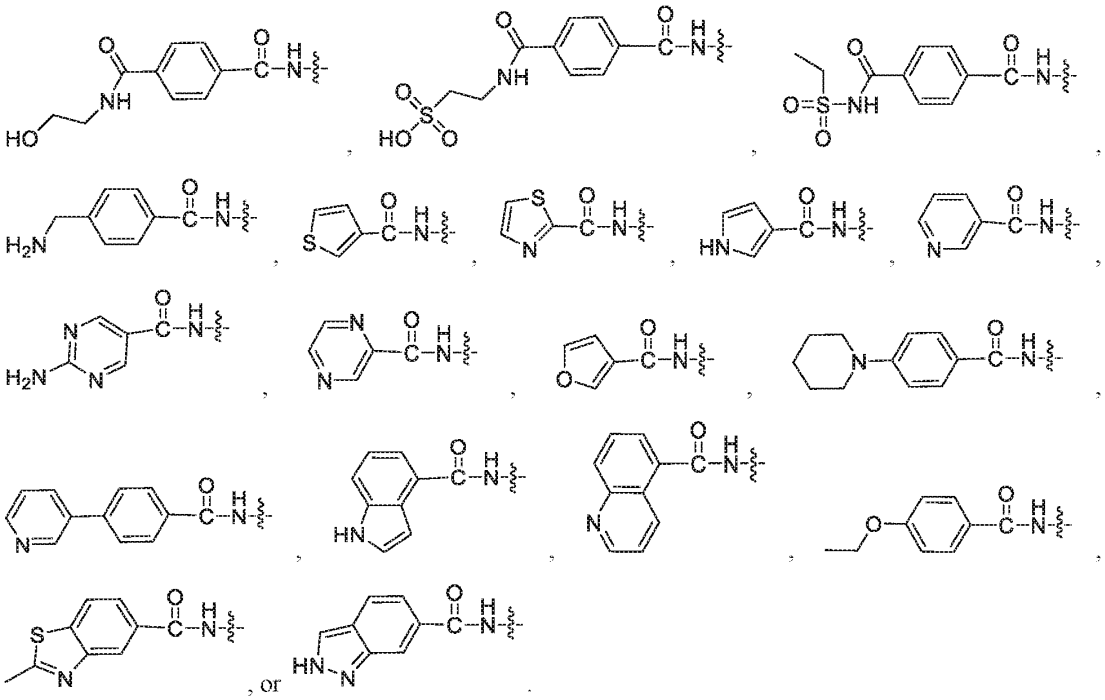
In some embodiments, is optionally substituted C_{1-6} alkyl. In some embodiments, R'' is $-OCH_3$. In some embodiments, $-X-R^L$ is $-N(R')C(O)OR^L$, wherein each of R' and R^L is independently as described herein. In some embodiments, R is . In some embodiments, $-X-R^L$ is $-NHC(O)OCH_3$. In some embodiments, $-X-R^L$ is $-NHC(O)N(CH_3)_2$. In some embodiments, a linkage is $-OP(O)(NHC(O)CH_3)O-$. In some embodiments, a linkage is $-OP(O)(NHC(O)OCH_3)O-$. In some embodiments, a linkage is $-OP(O)(NHC(O)(p\text{-methylphenyl}))O-$. In some embodiments, a linkage is $-OP(O)(NHC(O)N(CH_3)_2)O-$. In some embodiments, $-X-R^L$ is $-N(R')R^L$, wherein each of R' and R^L is independently as described herein. In some embodiments, $-X-R^L$ is $-N(R')R^L$, wherein each of R' and R^L is independently not hydrogen. In some embodiments, $-X-R^L$ is $-NHR^L$, wherein R^L is as described herein. In some embodiments, R^L is not hydrogen. In some embodiments, R^L is optionally substituted aryl or heteroaryl. In some embodiments, R^L is optionally substituted aryl. In some embodiments, R^L is optionally substituted phenyl. In some embodiments, $-X-R^L$ is $-N(R')_2$, wherein each R' is independently as described herein. In some embodiments, $-X-R^L$ is $-NHR'$, wherein R' is as described herein. In some embodiments, $-X-R^L$ is $-NHR$, wherein R is as described herein. In some embodiments, $-X-R^L$ is R^L, wherein R^L is as described herein. In some embodiments, R^L is $-N(R')_2$, wherein each R' is independently as described herein. In some embodiments, R^L is $-NHR'$, wherein R' is as described herein. In some embodiments, R^L is $-NHR$, wherein R is as described herein. In some embodiments, R^L is $-N(R')_2$, wherein each R' is independently as described herein. In some embodiments, none of R' in $-N(R')_2$ is hydrogen. In some embodiments, R^L is $-N(R')_2$, wherein each R' is independently C_{1-6} aliphatic. In some embodiments, R^L is $-L-R'$, wherein each of L and R' is independently as described herein. In some embodiments, R^L is $-L-R$, wherein each of L and R is independently as described herein. In some embodiments, R^L is $-N(R')-Cy-N(R')-R'$. In some embodiments, R^L is $-N(R')-Cy-C(O)-R'$. In some embodiments, R^L is $-N(R')-Cy-O-R'$. In some embodiments, R^L is $-N(R')-Cy-SO_2-R'$. In some embodiments, R^L is $-N(R')-Cy-SO_2-N(R')_2$. In some embodiments, R^L is $-N(R')-Cy-C(O)-N(R')_2$. In some embodiments, R^L is $-N(R')-Cy-OP(O)(R'')_2$. In some embodiments, $-Cy-$ is an optionally substituted bivalent aryl group. In some embodiments, $-Cy-$ is optionally substituted phenylene. In some embodiments, $-Cy-$ is optionally substituted 1,4-phenylene. In some embodiments, $-Cy-$ is 1,4-phenylene. In some embodiments, R^L is $-N(CH_3)_2$. In some embodiments, R^L is $-N(i\text{-}Pr)_2$. In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is

. In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is , , , , , , , , , , , ,



. In some embodiments, –X–R^L is –N(R')–C(O)–Cy–R^L. In some embodiments, –X–R^L is R^L. In some embodiments, R^L is –N(R')–C(O)–Cy–O–R'. In some embodiments, R^L is –N(R')–C(O)–Cy–R'. In some embodiments, R^L is –N(R')–C(O)–Cy–C(O)–R'. In some embodiments, R^L is –N(R')–C(O)–Cy–N(R')$_2$. In some embodiments, R^L is –N(R')–C(O)–Cy–SO_2–N(R')$_2$. In some embodiments, R^L is –N(R')–C(O)–Cy–C(O)–N(R')$_2$. In some embodiments, R^L is –N(R')–C(O)–Cy–C(O)–N(R')–SO_2–R'. In some embodiments, R' is R as described herein. In some embodiments, R^L is





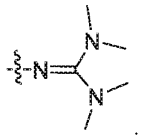
[00857] As described herein, in some embodiments, one or more methylene units of L, or a variable which comprises or is L, are independently replaced with −O−, −N(R')−, −C(O)−, −C(O)N(R')−, −SO_2−, −SO_2N(R')−, or −Cy−. In some embodiments, a methylene unit is replaced with −Cy−. In some embodiments, −Cy− is an optionally substituted bivalent aryl group. In some embodiments, −Cy− is optionally substituted phenylene. In some embodiments, −Cy− is optionally substituted 1,4-phenylene. In some embodiments, −Cy− is an optionally substituted bivalent 5-20 (e.g. 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) membered heteroaryl group having 1-10 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) heteroatoms. In some embodiments, −Cy− is monocyclic. In some embodiments, −Cy− is bicyclic. In some embodiments, −Cy− is polycyclic. In some embodiments, each monocyclic unit in −Cy− is independently 3-10 (e.g., 3, 4, 5, 6, 7, 8, 9, or 10) membered, and is independently saturated, partially saturated, or aromatic. In some embodiments, −Cy− is an optionally substituted 3-20 (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) membered monocyclic, bicyclic or polycyclic aliphatic group. In some embodiments, −Cy− is an optionally substituted 3-20 (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20) membered monocyclic, bicyclic or polycyclic heteroaliphatic group having 1-10 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) heteroatoms.

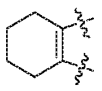
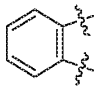
[00858] In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−N(R')P(O)(R")$_2$)−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−N(R')P(O)(R")$_2$)−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−N(R')P(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments,

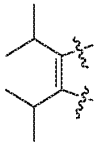
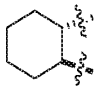
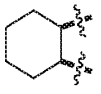
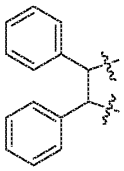
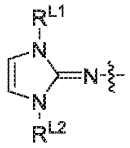
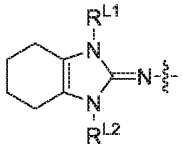
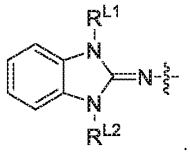
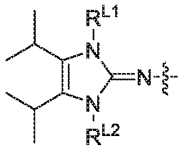
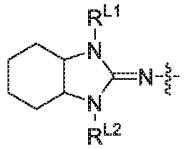
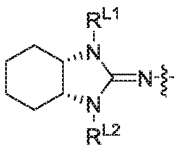
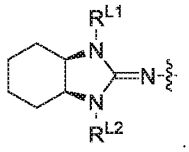
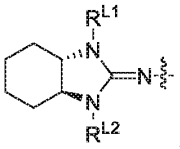
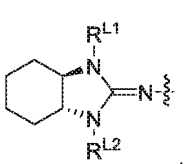
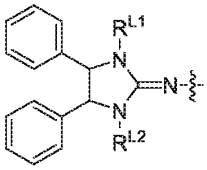
an internucleotidic linkage has the structure of −P(=S)(−N(R')P(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=O)(−N(R')P(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=S)(−N(R')P(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, R', e.g., of −N(R')−, is hydrogen or optionally substituted C_{1-6} aliphatic. In some embodiments, R' is C_{1-6} alkyl. In some embodiments, R' is hydrogen. In some embodiments, R", e.g., in −P(O)(R")$_2$, is R' as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−NHP(O)(R")$_2$)−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−NHP(O)(R")$_2$)−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=O)(−NHP(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −P(=S)(−NHP(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=O)(−NHP(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an internucleotidic linkage has the structure of −OP(=S)(−NHP(O)(R")$_2$)O−, wherein each R" is independently as described herein. In some embodiments, an occurrence of R", e.g., in −P(O)(R")$_2$, is R. In some embodiments, R is an optionally substituted group selected from C_{1-6} aliphatic, aryl, heterocyclyl, and heteroaryl. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted C_{1-6} alkenyl. In some embodiments, R is optionally substituted C_{1-6} alkynyl. In some embodiments, R is methyl. In some embodiments, R is optionally substituted methyl. In some embodiments, R is $-CF_3$. In some embodiments, R is optionally substituted ethyl. In some embodiments, R is ethyl. In some embodiments, R is $-CH_2CHF_2$. In some embodiments, R is $-CH_2CH_2OCH_3$. In some embodiments, R is optionally substituted C_{1-20} (e.g., C_{1-6}, C_{2-6}, C_{3-6}, C_{1-10}, C_{2-10}, C_{3-10}, C_{2-20}, C_{3-20}, C_{10-20}, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) aliphatic. In some embodiments, R is optionally substituted C_{1-20} (e.g., C_{1-6}, C_{2-6}, C_{3-6}, C_{1-10}, C_{2-10}, C_{3-10}, C_{2-20}, C_{3-20}, C_{10-20}, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) alkyl. In some embodiments, R is an optionally substituted linear C_{2-20} aliphatic. In some embodiments, R is optionally substituted linear C_{2-20} alkyl. In some embodiments, R is linear C_{2-20} alkyl. In some embodiments, R is isopropyl. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} aliphatic. In some embodiments, R is optionally substituted C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is optionally substituted linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, R is linear C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, or C_{20} alkyl. In some embodiments, each R" is independently R as described herein, for example, in some embodiments, each R" is methyl. In some embodiments, R" is optionally substituted aryl. In some embodiments, R is optionally substituted phenyl. In

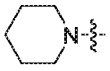
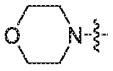
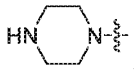
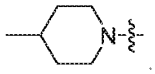
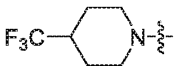
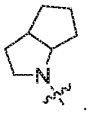
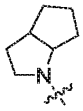
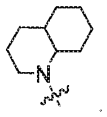
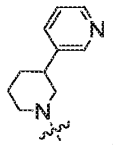
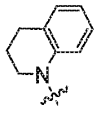
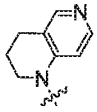
some embodiments, R is p-methylphenyl. In some embodiments, R is benzyl. In some embodiments, R is optionally substituted heteroaryl. In some embodiments, R is optionally substituted 1,3-diazolyl. In some embodiments, R is optionally substituted 2-(1,3)-diazolyl. In some embodiments, R is optionally substituted 1-methyl-2-(1,3)-diazolyl. In some embodiments, an occurrence of R" is $-N(R')_2$. In some embodiments, R" is $-N(CH_3)_2$. In some embodiments, an occurrence of R", e.g., in $-P(O)(R")_2$, is $-OR'$, wherein R' is as described herein. In some embodiments, R' is R as described herein. In some embodiments, is optionally substituted C_{1-6} aliphatic. In some embodiments, is optionally substituted C_{1-6} alkyl. In some embodiments, R" is $-OCH_3$. In some embodiments, each R" is $-OR'$ as described herein. In some embodiments, each R" is $-OCH_3$. In some embodiments, each R" is $-OH$. In some embodiments, a linkage is $-OP(O)(NHP(O)(OH)_2)O-$. In some embodiments, a linkage is $-OP(O)(NHP(O)(OCH_3)_2)O-$. In some embodiments, a linkage is $-OP(O)(NHP(O)(CH_3)_2)O-$.

[00859] In some embodiments, $-N(R")_2$ is $-N(R')_2$. In some embodiments, $-N(R")_2$ is $-NHR$. In some embodiments, $-N(R")_2$ is $-NHC(O)R$. In some embodiments, $-N(R")_2$ is $-NHC(O)OR$. In some embodiments, $-N(R")_2$ is $-NHS(O)_2R$.

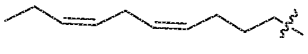
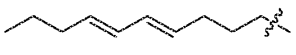
[00860] In some embodiments, an internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, an internucleotidic linkage comprises $-X-R^L$ as described herein. In some embodiments, $-X-R^L$ is $-N=C(-L^L-R^L)_2$. In some embodiments, $-X-R^L$ is $-N=C[N(R^L)_2]_2$. In some embodiments, $-X-R^L$ is $-N=C[NR'R^L]_2$. In some embodiments, $-X-R^L$ is $-N=C[N(R')_2]_2$. In some embodiments, $-X-R^L$ is $-N=C[N(R^L)_2](CHR^{L1}R^{L2})$, wherein each of R^{L1} and R^{L2} is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C(NR'R^L)(CHR^{L1}R^{L2})$, wherein each of R^{L1} and R^{L2} is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C(NR'R^L)(CR'R^{L1}R^{L2})$, wherein each of R^{L1} and R^{L2} is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C[N(R')_2](CHR'R^{L2})$. In some embodiments, $-X-R^L$ is $-N=C[N(R^L)_2](R^L)$. In some embodiments, $-X-R^L$ is $-N=C(NR'R^L)(R^L)$. In some embodiments, $-X-R^L$ is $-N=C(NR'R^L)(R')$. In some embodiments, $-X-R^L$ is $-N=C[N(R')_2](R')$. In some embodiments, $-X-R^L$ is $-N=C(NR'R^{L1})(NR'R^{L2})$, wherein each R^{L1} and R^{L2} is independently R^L, and each R' and R^L is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C(NR'R^{L1})(NR'R^{L2})$, wherein variable is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C(NR'R^{L1})(CHR'R^{L2})$, wherein variable is independently as described herein. In some embodiments, $-X-R^L$ is $-N=C(NR'R^{L1})(R')$, wherein variable is independently as described herein. In some embodiments, each R' is independently R. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl. In some embodiments, $-X-R^L$ is . In some embodiments, two groups selected from R', R^L, R^{L1}, R^{L2}, etc. (in some embodiments, on the same atom (e.g., $-N(R')_2$, or $-NR'R^L$, or $-N(R^L)^2$, wherein R' and R^L can independently be R as described herein), etc.), or on

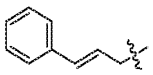
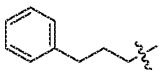
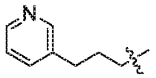
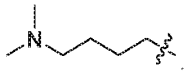
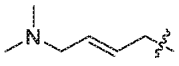
different atoms (e.g., the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$) or –N=C(N**R'**R^{L1})(N**R'**R^{L2}); can also be two other variables that can be R, e.g., R^L, R^{L1}, R^{L2}, etc.)) are independently R and are taken together with their intervening atoms to form a ring as described herein. In some embodiments, two of R, R', R^L, R^{L1}, or R^{L2} on the same atom, e.g., of $-N(R')_2$, $-N(R^L)_2$, $-NR'R^L$, $-NR'R^{L1}$, $-NR'R^{L2}$, $-CR'R^{L1}R^{L2}$, etc., are taken together to form a ring as described herein. In some embodiments, two R', R^L, R^{L1}, or R^{L2} on two different atoms, e.g., the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$), –N=C(N**R'**R^{L1})(N**R'**R^{L2}), etc. are taken together to form a ring as described herein. In some embodiments, a formed ring is an optionally substituted 3-20 (e.g., 3-15, 3-12, 3-10, 3-9, 3-8, 3-7, 3-6, 4-15, 4-12, 4-10, 4-9, 4-8, 4-7, 4-6, 5-15, 5-12, 5-10, 5-9, 5-8, 5-7, 5-6, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) monocyclic, bicyclic or tricyclic ring having 0-5 additional heteroatoms. In some embodiments, a formed ring is monocyclic as described herein. In some embodiments, a formed ring is an optionally substituted 5-10 membered monocyclic ring. In some embodiments, a formed ring is bicyclic. In some embodiments, a formed ring is polycyclic. In some embodiments, two groups that are or can be R (e.g., the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$) or –N=C(N**R'**R^{L1})(N**R'**R^{L2}), the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$), –N=C(N**R'**R^{L1})(N**R'**R^{L2}), etc.) are taken together to form an optionally substituted bivalent hydrocarbon chain, e.g., an optionally substituted C_{1-20} aliphatic chain, optionally substituted $-(CH_2)n-$ wherein n is 1-20 (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20). In some embodiments, a hydrocarbon chain is saturated. In some embodiments, a hydrocarbon chain is partially unsaturated. In some embodiments, a hydrocarbon chain is unsaturated. In some embodiments, two groups that are or can be R (e.g., the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$) or –N=C(N**R'**R^{L1})(N**R'**R^{L2}), the two **R'** in –N=C(N**R'**R^L)(C**R'**$R^{L1}R^{L2}$), –N=C(N**R'**R^{L1})(N**R'**R^{L2}), etc.) are taken together to form an optionally substituted bivalent heteroaliphatic chain, e.g., an optionally substituted C_{1-20} heteroaliphatic chain having 1-10 heteroatoms. In some embodiments, a heteroaliphatic chain is saturated. In some embodiments, a heteroaliphatic chain is partially unsaturated. In some embodiments, a heteroaliphatic chain is unsaturated. In some embodiments, a chain is optionally substituted $-(CH_2)-$. In some embodiments, a chain is optionally substituted $-(CH_2)_2-$. In some embodiments, a chain is optionally substituted $-(CH_2)-$. In some embodiments, a chain is optionally substituted $-(CH_2)_2-$. In some embodiments, a chain is optionally substituted $-(CH_2)_3-$. In some embodiments, a chain is optionally substituted $-(CH_2)_4-$. In some embodiments, a chain is optionally substituted $-(CH_2)_5-$. In some embodiments, a chain is optionally substituted $-(CH_2)_6-$. In some embodiments, a chain is optionally substituted –CH=CH–. In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally

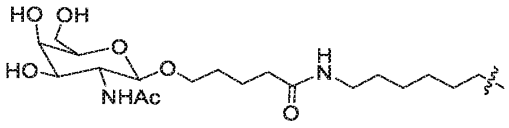
substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, a chain is optionally substituted . In some embodiments, two of R, R', R^L, R^{L1}, R^{L2}, etc. on different atoms are taken together to form a ring as described herein. For examples, in some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-N(R')_2$, $-N(R)_2$, $-N(R^L)_2$, $-NR'R^L$, $-NR'R^{L1}$, $-NR'R^{L2}$, $-NR^{L1}R^{L2}$, etc. is a formed ring. In

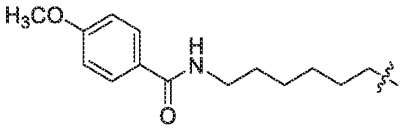
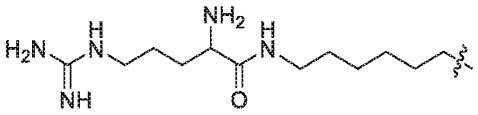
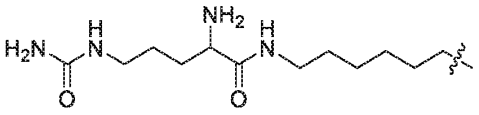
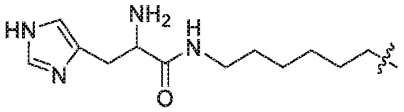
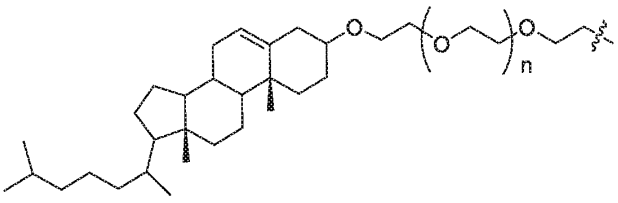
some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted . In some embodiments, a ring is optionally substituted .

[00861] In some embodiments, R^{L1} and R^{L2} are the same. In some embodiments, R^{L1} and R^{L2} are different. In some embodiments, each of R^{L1} and R^{L2} is independently R^L as described herein, e.g., below.

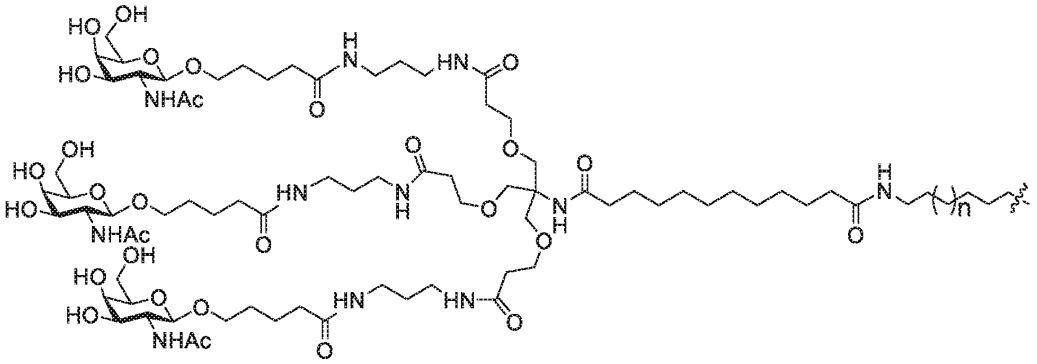
[00862] In some embodiments, R^L is optionally substituted C_{1-30} aliphatic. In some embodiments, R^L is optionally substituted C_{1-30} alkyl. In some embodiments, R^L is linear. In some embodiments, R^L is optionally substituted linear C_{1-30} alkyl. In some embodiments, R^L is optionally substituted C_{1-6} alkyl. In some embodiments, R^L is methyl. In some embodiments, R^L is ethyl. In some embodiments, R^L is n-propyl. In some embodiments, R^L is isopropyl. In some embodiments, R^L is n-butyl. In some embodiments, R^L is tert-butyl. In some embodiments, R^L is (E)–CH_2–CH=CH–CH_2–CH_3. In some embodiments, R^L is (Z)–CH_2–CH=CH–CH_2–CH_3. In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is $CH_3(CH_2)_2C \equiv CC \equiv$

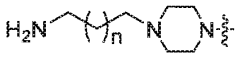
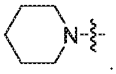
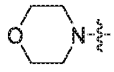
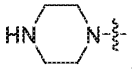
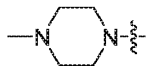
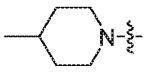
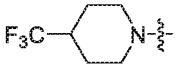
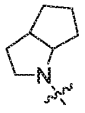
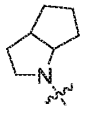
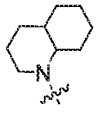
$C(CH_2)_3-$. In some embodiments, R^L is $CH_3(CH_2)_5C\equiv C-$. In some embodiments, R^L optionally substituted aryl. In some embodiments, R^L is optionally substituted phenyl. In some embodiments, R^L is phenyl substituted with one or more halogen. In some embodiments, R^L is phenyl optionally substituted with halogen, $-N(R')$, or $-N(R')C(O)R'$. In some embodiments, R^L is phenyl optionally substituted with $-Cl$, $-Br$, $-F$, $-N(Me)_2$, or $-NHCOCH_3$. In some embodiments, R^L is $-L^L-R'$, wherein L^L is an optionally substituted C_{1-20} saturated, partially unsaturated or unsaturated hydrocarbon chain. In some embodiments, such a hydrocarbon chain is linear. In some embodiments, such a hydrocarbon chain is unsubstituted. In some embodiments, L^L is $(E)-CH_2-CH=CH-$. In some embodiments, L^L is $-CH_2-C\equiv C-CH_2-$. In some embodiments, L^L is $-(CH_2)_3-$. In some embodiments, L^L is $-(CH_2)_4-$. In some embodiments, L^L is $-(CH_2)_n-$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R' is optionally substituted aryl as described herein. In some embodiments, R' is optionally substituted phenyl. In some embodiments, R' is phenyl. In some embodiments, R' is optionally substituted heteroaryl as described herein. In some embodiments, R' is 2'-pyridinyl. In some embodiments, R' is 3'-pyridinyl. In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is $-L^L-N(R')_2$, wherein each variable is independently as described herein. In some embodiments, each R' is independently C_{1-6} aliphatic as described herein. In some embodiments, $-N(R')_2$ is $-N(CH_3)_2$. In some embodiments, $-N(R')_2$ is $-NH_2$. In some embodiments, R^L is $-(CH_2)_n-N(R')_2$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R^L is $-(CH_2CH_2O)_n-CH_2CH_2-N(R')_2$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is $-(CH_2)_n-NH_2$. In some embodiments, R^L is $-(CH_2CH_2O)_n-CH_2CH_2-NH_2$. In some embodiments, R^L is $-(CH_2CH_2O)_n-CH_2CH_2-R'$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R^L is $-(CH_2CH_2O)_n-CH_2CH_2CH_3$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R^L is $-(CH_2CH_2O)_n-CH_2CH_2OH$, wherein n is 1-30 (e.g., 1-20, 5-30, 6-30, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, etc.). In some embodiments, R^L is or comprises a carbohydrate moiety, e.g., GalNAc. In some embodiments,

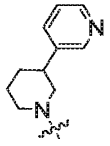
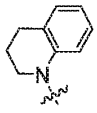
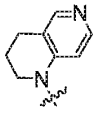


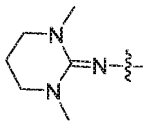
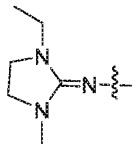
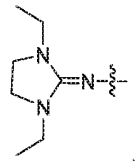
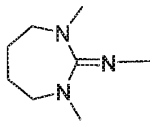
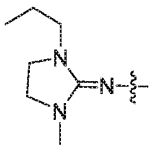
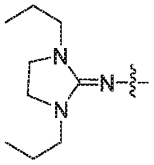
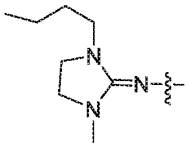
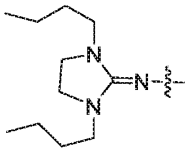
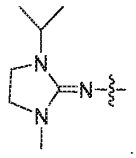
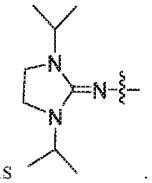
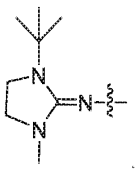
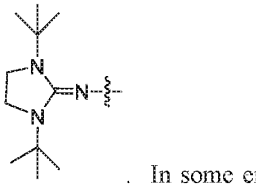
R^L is $-L^L$–GalNAc. In some embodiments, R^L is . In some embodiments, one or more methylene units of L^L are independently replaced with –Cy– (e.g., optionally substituted 1,4-phenylene, a 3-30 membered bivalent optionally substituted monocyclic, bicyclic, or polycyclic cycloaliphatic ring, etc.), –O–, –N(R')– (e.g., –NH), –C(O)–, –C(O)N(R')– (e.g., –C(O)NH–), –C(NR')– (e.g., –C(NH)–), –N(R')C(O)(N(R')– (e.g., –NHC(O)NH–), –N(R')C(NR')(N(R')– (e.g., –NHC(NH)NH–), $-(CH_2CH_2O)_n$–, etc. For example, in some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is . In some embodiments, R^L is 

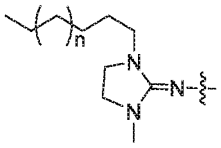
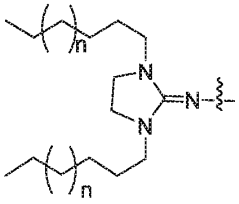
wherein n is 0-20. In some embodiments, R^L is or comprises one or more additional chemical moieties (e.g., carbohydrate moieties, GalNAc moieties, etc.) optionally substituted connected through a linker (which can be bivalent or polyvalent). For example, in some embodiments, R^L is

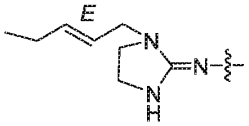


wherein n is 0-20. In some embodiments, R^L is , wherein n is 0-20. In some embodiments, R^L is R' as described herein. As described herein, many variable can independently be R'. In some embodiments, R' is R as described herein. As described herein, various variables can independently be R. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is methyl. In some embodiments, R is optionally substituted cycloaliphatic. In some embodiments, R is optionally substituted cycloalkyl. In some embodiments, R is optionally substituted aryl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is optionally substituted heteroaryl. In some embodiments, R is optionally substituted heterocyclyl. In some embodiments, R is optionally substituted C_{1-20} heterocyclyl having 1-5 heteroatoms, e.g., one of which is nitrogen. In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted 

. In some embodiments, R is optionally substituted  . In some embodiments, R is optionally substituted  . In some embodiments, R is optionally substituted  .

[00863] In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is  . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is  .


, wherein n is 1-20. In some embodiments, –X–R^L is 
, wherein n is 1-20. In some embodiments, –X–R^L is selected from: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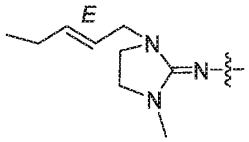
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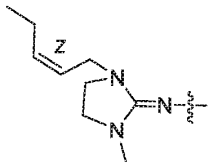
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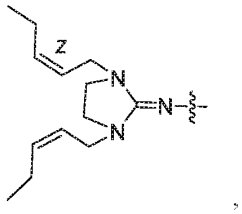
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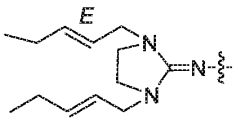
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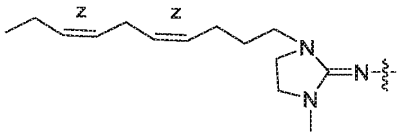
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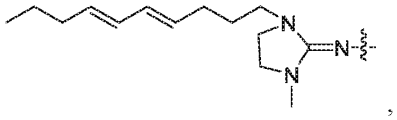
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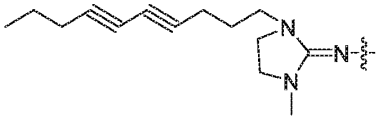
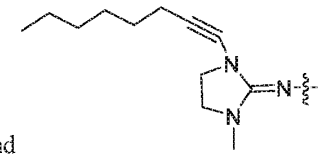
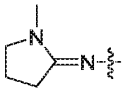
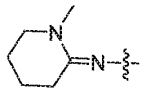
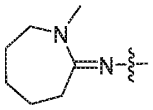

and

. In some embodiments, –X–R^L is

. In some embodiments, –X–R^L is

. In some embodiments, –X–R^L is

.

[00864] In some embodiments, R^L is R" as described herein. In some embodiments, R^L is R as described herein.

[00865] In some embodiments, R" or R^L is or comprises an additional chemical moiety. In some embodiments, R" or R^L is or comprises an additional chemical moiety, wherein the additional chemical moiety is or comprises a carbohydrate moiety. In some embodiments, R" or R^L is or comprises a GalNAc. In some embodiments, R^L or R" is replaced with, or is utilized to connect to, an additional chemical moiety.

[00866] In some embodiments, X is –O–. In some embodiments, X is –S–. In some embodiments, X is –L^L–N(–L^L–R^L)–L^L–. In some embodiments, X is –N(–L^L–R^L)–L^L–. In some embodiments, X is –L^L–N(–L^L–R^L)–. In some embodiments, X is –N(–L^L–R^L)–. In some embodiments, X is –L^L–N=C(–L^L–R^L)–L^L–. In some embodiments, X is –N=C(–L^L–R^L)–L^L–. In some embodiments, X is –L^L–N=C(–L^L–R^L)–. In some embodiments, X is –N=C(–L^L–R^L)–. In some embodiments, X is L^L. In some embodiments, X is a covalent

bond.

[00867] In some embodiments, Y is a covalent bond. In some embodiments, Y is −O−. In some embodiments, Y is −N(R')−. In some embodiments, Z is a covalent bond. In some embodiments, Z is −O−. In some embodiments, Z is −N(R')−. In some embodiments, R' is R. In some embodiments, R is −H. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl. In some embodiments, R is ethyl. In some embodiments, R is propyl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl.

[00868] As described herein, various variables in structures in the present disclosure can be or comprise R. Suitable embodiments for R are described extensively in the present disclosure. As appreciated by those skilled in the art, R embodiments described for a variable that can be R may also be applicable to another variable that can be R. Similarly, embodiments described for a component/moiety (e.g., L) for a variable may also be applicable to other variables that can be or comprise the component/moiety.

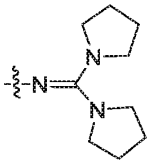
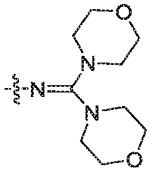
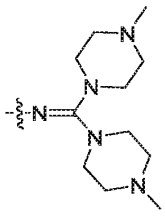
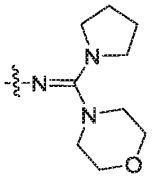
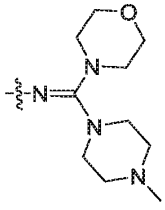
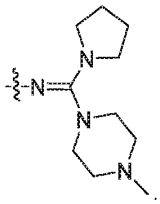
[00869] In some embodiments, R" is R'. In some embodiments, R" is $-N(R')_2$.

[00870] In some embodiments, $-X-R^L$ is −SH. In some embodiments, $-X-R^L$ is −OH.

[00871] In some embodiments, $-X-R^L$ is $-N(R')_2$. In some embodiments, each R' is independently optionally substituted C_{1-6} aliphatic. In some embodiments, each R' is independently methyl.

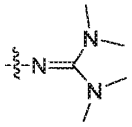
[00872] In some embodiments, a non-negatively charged internucleotidic linkage has the structure of $-OP(=O)(-N=C((N(R')_2)_2-O-$. In some embodiments, a R' group of one $N(R')_2$ is R, a R' group of the other $N(R')_2$ is R, and the two R groups are taken together with their intervening atoms to form an optionally substituted ring, e.g., a 5-membered ring as in n001. In some embodiments, each R' is independently R, wherein each R is independently optionally substituted C_{1-6} aliphatic.

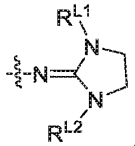
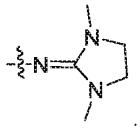
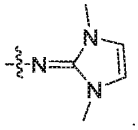
[00873] In some embodiments, $-X-R^L$ is $-N=C(-L^L-R')_2$. In some embodiments, $-X-R^L$ is $-N=C(-L^{L1}-L^{L2}-L^{L3}-R')_2$, wherein each L^{L1}, L^{L2} and L^{L3} is independently L", wherein each L" is independently a covalent bond, or a bivalent, optionally substituted, linear or branched group selected from a C_{1-10} aliphatic group and a C_{1-10} heteroaliphatic group having 1-5 heteroatoms, wherein one or more methylene units are optionally and independently replaced by an optionally substituted group selected from C_{1-6} alkylene, C_{1-6} alkenylene, —C≡C—, a bivalent C_1–C_6 heteroaliphatic group having 1-5 heteroatoms, $-C(R')_2-$, −Cy−, −O−, −S−, −S−S−, −N(R')−, −C(O)−, −C(S)−, −C(NR')−, −C(O)N(R')−, −N(R')C(O)N(R')−, −N(R')C(O)O−, −S(O)−, $-S(O)_2-$, $-S(O)_2N(R')-$, −C(O)S−, −C(O)O−, −P(O)(OR')−, −P(O)(SR')−, −P(O)(R')−, −P(O)(NR')−, −P(S)(OR')−, −P(S)(SR')−, −P(S)(R')−, −P(S)(NR')−, −P(R')−, −P(OR')−, −P(SR')−, −P(NR')−, $-P(OR')[B(R')_3]-$, −OP(O)(OR')O−, −OP(O)(SR')O−, −OP(O)(R')O−, −OP(O)(NR')O−, −OP(OR')O−, −OP(SR')O−, −OP(NR')O−, −OP(R')O−, or $-OP(OR')[B(R')_3]O-$, and one or more nitrogen or carbon atoms are optionally and independently replaced with Cy^L. In some embodiments, L^{L2} is −Cy−. In some embodiments, L^{L1} is a covalent bond. In some embodiments, L^{L3} is a covalent bond. In some

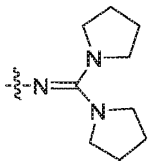
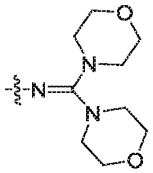
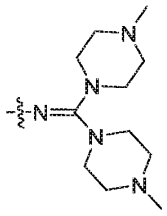
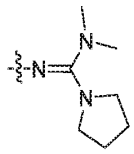
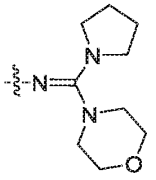
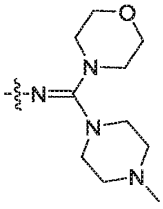
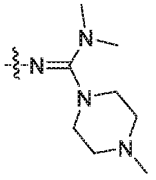
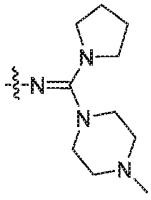
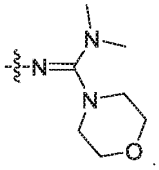
embodiments, $-X-R^L$ is $-N=C(-L^{L1}-Cy-L^{L3}-R')_2$. In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is . In some embodiments, $-X-R^L$ is .

[00874] In some embodiments, as utilized in the present disclosure, L is covalent bond. In some embodiments, L is a bivalent, optionally substituted, linear or branched group selected from a C_{1-30} aliphatic group and a C_{1-30} heteroaliphatic group having 1-10 heteroatoms, wherein one or more methylene units are optionally and independently replaced by an optionally substituted group selected from C_{1-6} alkylene, C_{1-6} alkenylene, $-C\equiv C-$, a bivalent C_1–C_6 heteroaliphatic group having 1-5 heteroatoms, $-C(R')_2-$, $-Cy-$, $-O-$, $-S-$, $-S-S-$, $-N(R')-$, $-C(O)-$, $-C(S)-$, $-C(NR')-$, $-C(O)N(R')-$, $-N(R')C(O)N(R')-$, $-N(R')C(O)O-$, $-S(O)-$, $-S(O)_2-$, $-S(O)_2N(R')-$, $-C(O)S-$, $-C(O)O-$, $-P(O)(OR')-$, $-P(O)(SR')-$, $-P(O)(R')-$, $-P(O)(NR')-$, $-P(S)(OR')-$, $-P(S)(SR')-$, $-P(S)(R')-$, $-P(S)(NR')-$, $-P(R')-$, $-P(OR')-$, $-P(SR')-$, $-P(NR')-$, $-P(OR')[B(R')_3]-$, $-OP(O)(OR')O-$, $-OP(O)(SR')O-$, $-OP(O)(R')O-$, $-OP(O)(NR')O-$, $-OP(OR')O-$, $-OP(SR')O-$, $-OP(NR')O-$, $-OP(R')O-$, or $-OP(OR')[B(R')_3]O-$, and one or more nitrogen or carbon atoms are optionally and independently replaced with Cy^L. In some embodiments, L is a bivalent, optionally substituted, linear or branched group selected from a C_{1-30} aliphatic group and a C_{1-30} heteroaliphatic group having 1-10 heteroatoms, wherein one or more methylene units are optionally and independently replaced by an optionally substituted group selected from $-C\equiv C-$, $-C(R')_2-$, $-Cy-$, $-O-$, $-S-$, $-S-S-$, $-N(R')-$, $-C(O)-$, $-C(S)-$, $-C(NR')-$, $-C(O)N(R')-$, $-N(R')C(O)N(R')-$, $-N(R')C(O)O-$, $-S(O)-$, $-S(O)_2-$, $-S(O)_2N(R')-$, $-C(O)S-$, $-C(O)O-$, $-P(O)(OR')-$, $-P(O)(SR')-$, $-P(O)(R')-$, $-P(O)(NR')-$,

–P(S)(OR')–, –P(S)(SR')–, –P(S)(R')–, –P(S)(NR')–, –P(R')–, –P(OR')–, –P(SR')–, –P(NR')–, –P(OR')[B(R')$_3$]–, –OP(O)(OR')O–, –OP(O)(SR')O–, –OP(O)(R')O–, –OP(O)(NR')O–, –OP(OR')O–, –OP(SR')O–, –OP(NR')O–, –OP(R')O–, or –OP(OR')[B(R')$_3$]O–, and one or more nitrogen or carbon atoms are optionally and independently replaced with Cy^L. In some embodiments, L is a bivalent, optionally substituted, linear or branched group selected from a C_{1-10} aliphatic group and a C_{1-10} heteroaliphatic group having 1-10 heteroatoms, wherein one or more methylene units are optionally and independently replaced by an optionally substituted group selected from —C≡C—, –C(R')$_2$–, –Cy–, –O–, –S–, –S–S–, –N(R')–, –C(O)–, –C(S)–, –C(NR')–, –C(O)N(R')–, –N(R')C(O)N(R')–, –N(R')C(O)O–, –S(O)–, –S(O)$_2$–, –S(O)$_2$N(R')–, –C(O)S–, –C(O)O–, –P(O)(OR')–, –P(O)(SR')–, –P(O)(R')–, –P(O)(NR')–, –P(S)(OR')–, –P(S)(SR')–, –P(S)(R')–, –P(S)(NR')–, –P(R')–, –P(OR')–, –P(SR')–, –P(NR')–, –P(OR')[B(R')$_3$]–, –OP(O)(OR')O–, –OP(O)(SR')O–, –OP(O)(R')O–, –OP(O)(NR')O–, –OP(OR')O–, –OP(SR')O–, –OP(NR')O–, –OP(R')O–, or –OP(OR')[B(R')$_3$]O–, and one or more nitrogen or carbon atoms are optionally and independently replaced with Cy^L. In some embodiments, one or more methylene units are optionally and independently replaced by an optionally substituted group selected from —C≡C—, –C(R')$_2$–, –Cy–, –O–, –S–, –S–S–, –N(R')–, –C(O)–, –C(S)–, –C(NR')–, –C(O)N(R')–, –N(R')C(O)N(R')–, –N(R')C(O)O–, –S(O)–, –S(O)$_2$–, –S(O)$_2$N(R')–, –C(O)S–, or –C(O)O–.

[00875] In some embodiments, an internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, –X–R^L is –N=C[N(R')$_2$]$_2$. In some embodiments, each R' is independently R. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is methyl. In some embodiments, –X–R^L is . In some embodiments, one R' on a nitrogen atom is taken with a R' on the other nitrogen to form a ring as described herein.

[00876] In some embodiments, –X–R^L is , wherein R^1 and R^2 are independently R'. In some embodiments, –X–R^L is . In some embodiments, –X–R^L is . In some embodiments, two R' on the same nitrogen are taken together to form a ring as described herein. In some embodiments,

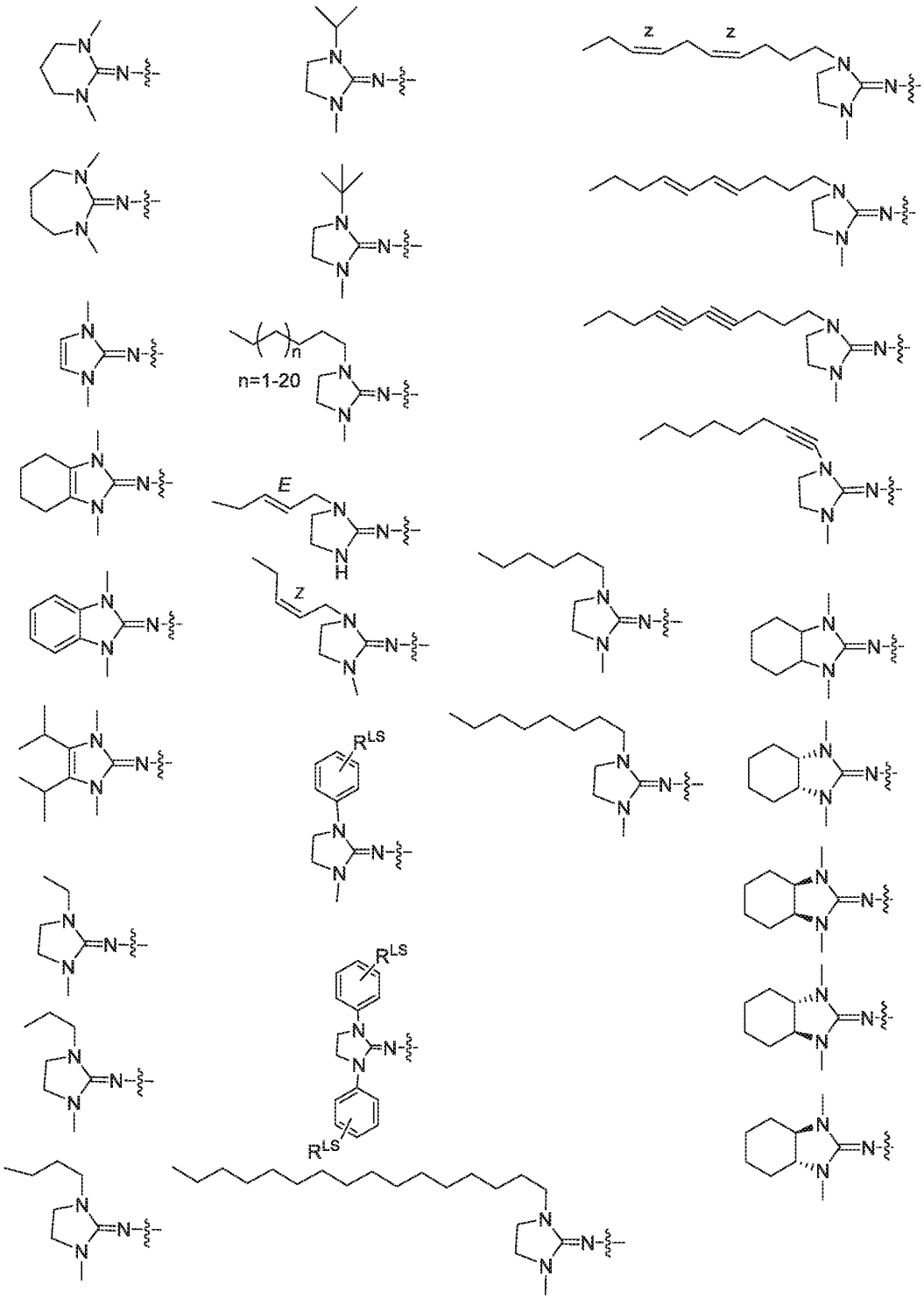
−X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is . In some embodiments, −X−R^L is .

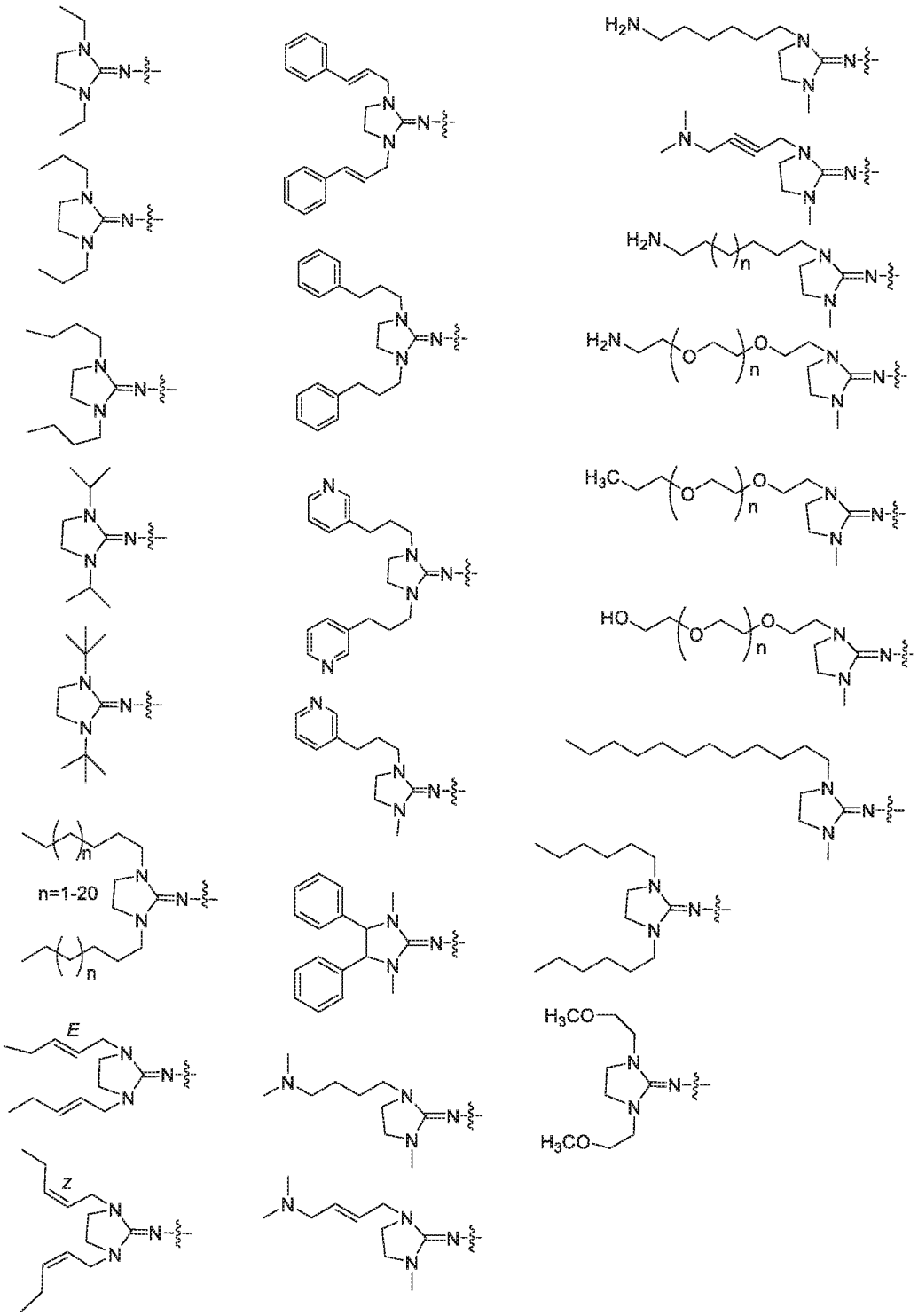
[00877] In some embodiments, −X−R^L is R as described herein. In some embodiments, R is not hydrogen. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is methyl.

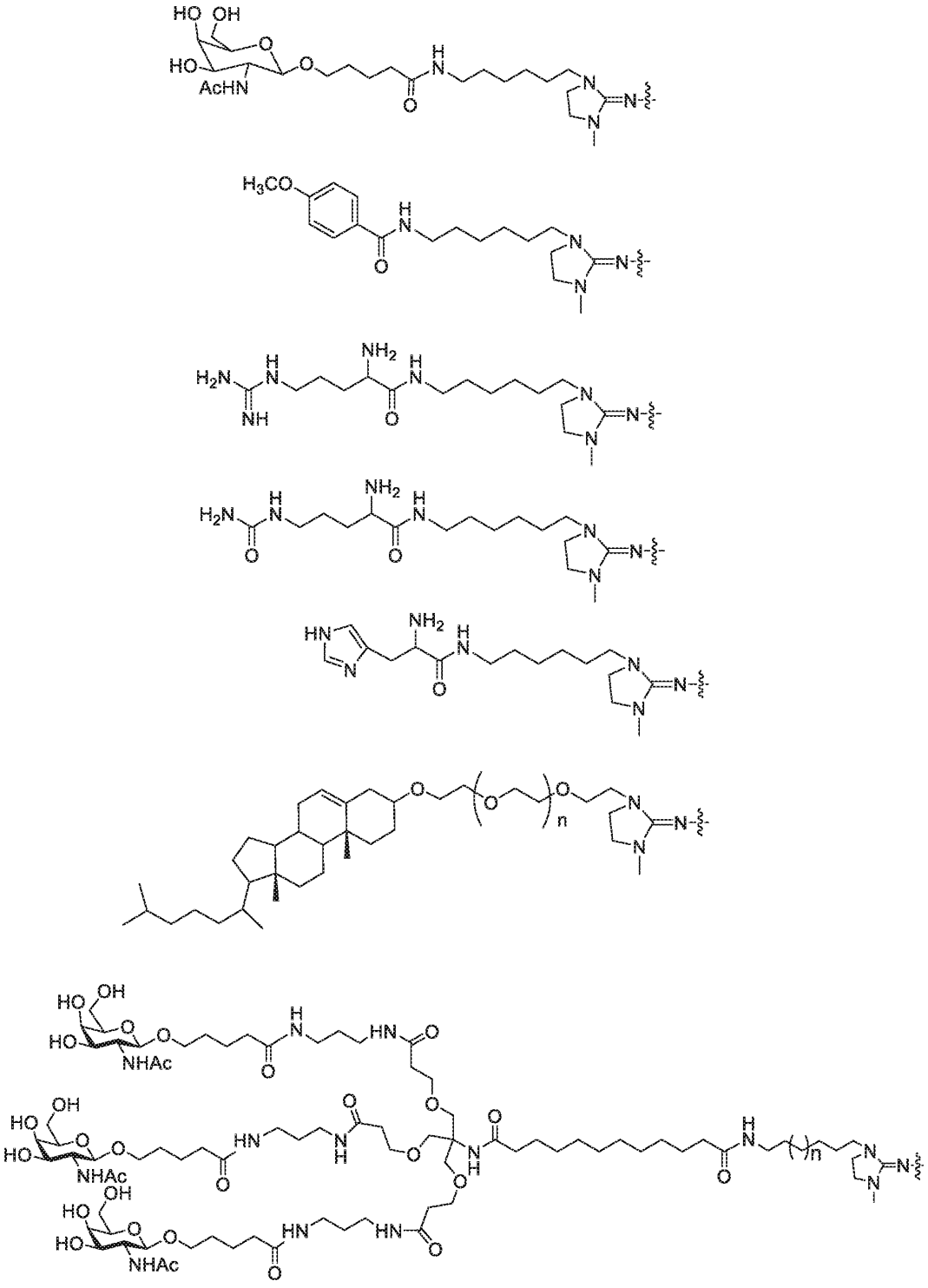
[00878] In some embodiments, −X−R^L is selected from Tables below. In some embodiments, X is as described herein. In some embodiments, R^L is as described herein. In some embodiments, a linkage has the structure of −Y−P^L(−X−R^L)−Z−, wherein −X−R^L is selected from Tables below, and each other variable is independently as described herein. In some embodiments, a linkage has the structure of or comprises −P(O)(−X−R^L)−, wherein −X−R^L is selected from Tables below. In some embodiments, a linkage has the structure of or comprises −P(S)(−X−R^L)−, wherein −X−R^L is selected from Tables below. In some embodiments, a linkage has the structure of or comprises −P(−X−R^L)−, wherein −X−R^L is selected from Tables below. In some embodiments, a linkage has the structure of or comprises −P(O)(−X−R^L)−O−, wherein −X−R^L

is selected from Tables below. In some embodiments, a linkage has the structure of or comprises $-P(S)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of or comprises $-P(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-P(O)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-P(S)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-P(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, P is bonded to a nitrogen atom (e.g., a nitrogen atom in sm01, sm18, etc.). In some embodiments, a linkage has the structure of or comprises $-O-P(O)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of or comprises $-O-P(S)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of or comprises $-O-P(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-O-P(O)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-O-P(S)(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, a linkage has the structure of $-O-P(-X-R^L)-O-$, wherein $-X-R^L$ is selected from Tables below. In some embodiments, the Tables below, n is 0-20 or as described herein. As those skilled in the art appreciate, a linkage may exist in a salt form.

Table L-1. Certain useful moieties bonded to linkage phosphorus (e.g., $-X-R^L$).


n=1-20
E
Z
Z
Z
R^LS
R^LS
R^LS


n=1-20
E
Z



wherein each R^{LS} is independently R^{s}. In some embodiments, each R^{LS} is independently −Cl, −Br, −F,

–N(Me)$_2$, or –NHCOCH$_3$.

Table L-2. Certain useful moieties bonded to linkage phosphorus (e.g., –X–R^L).

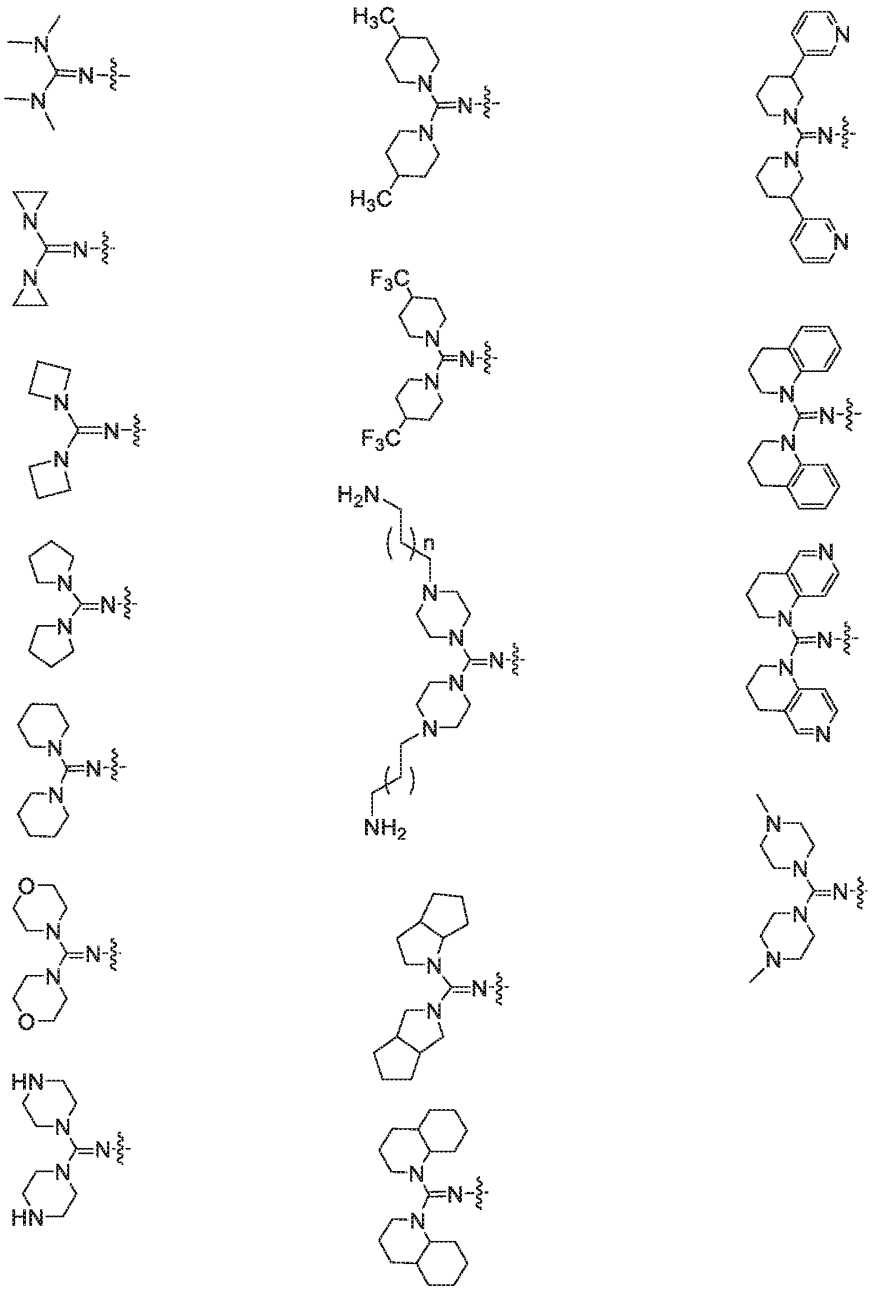


Table L-3. Certain useful moieties bonded to linkage phosphorus (e.g., –X–R^L).

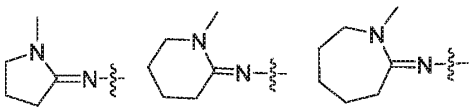
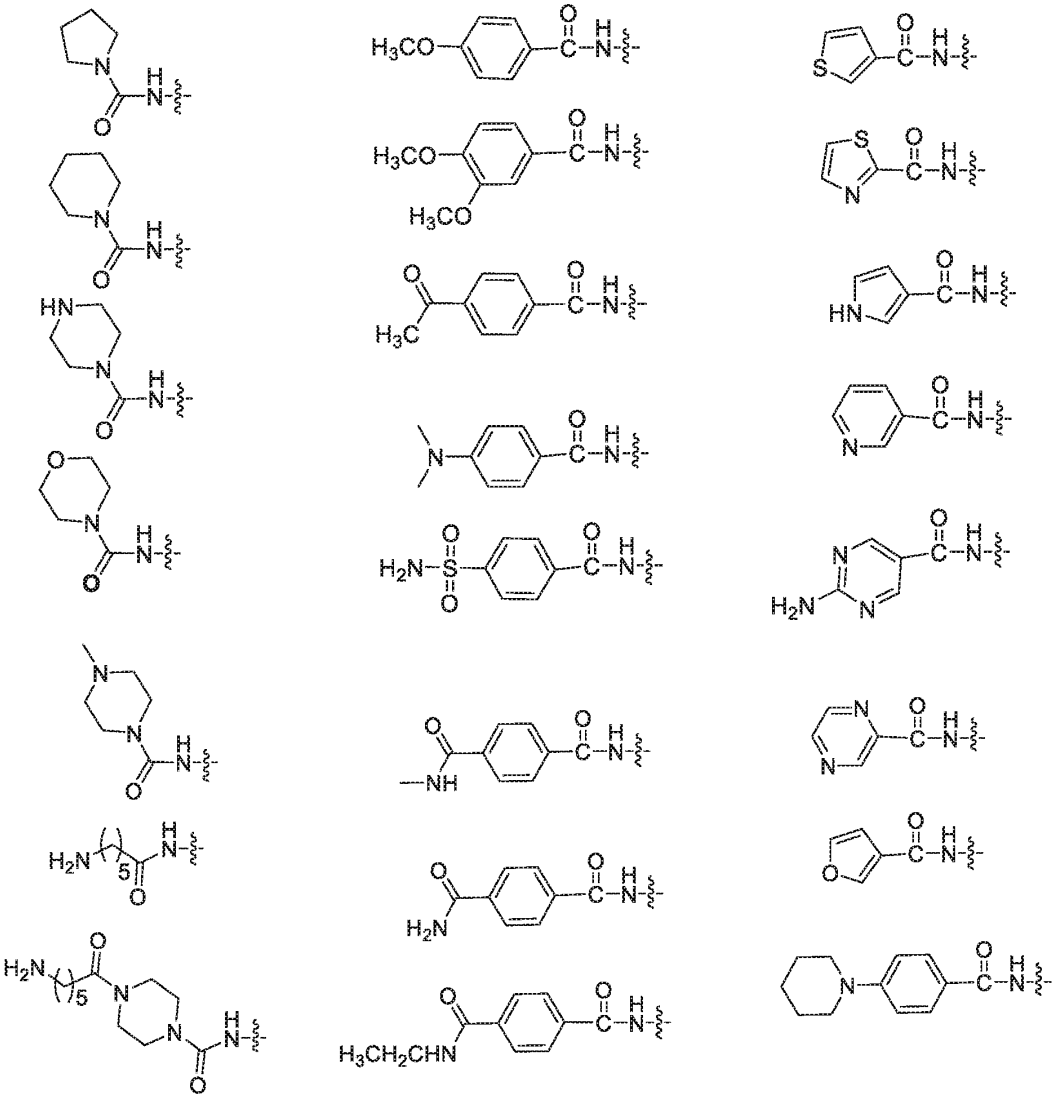


Table L-4. Certain useful moieties bonded to linkage phosphorus (e.g., −X−R^L).



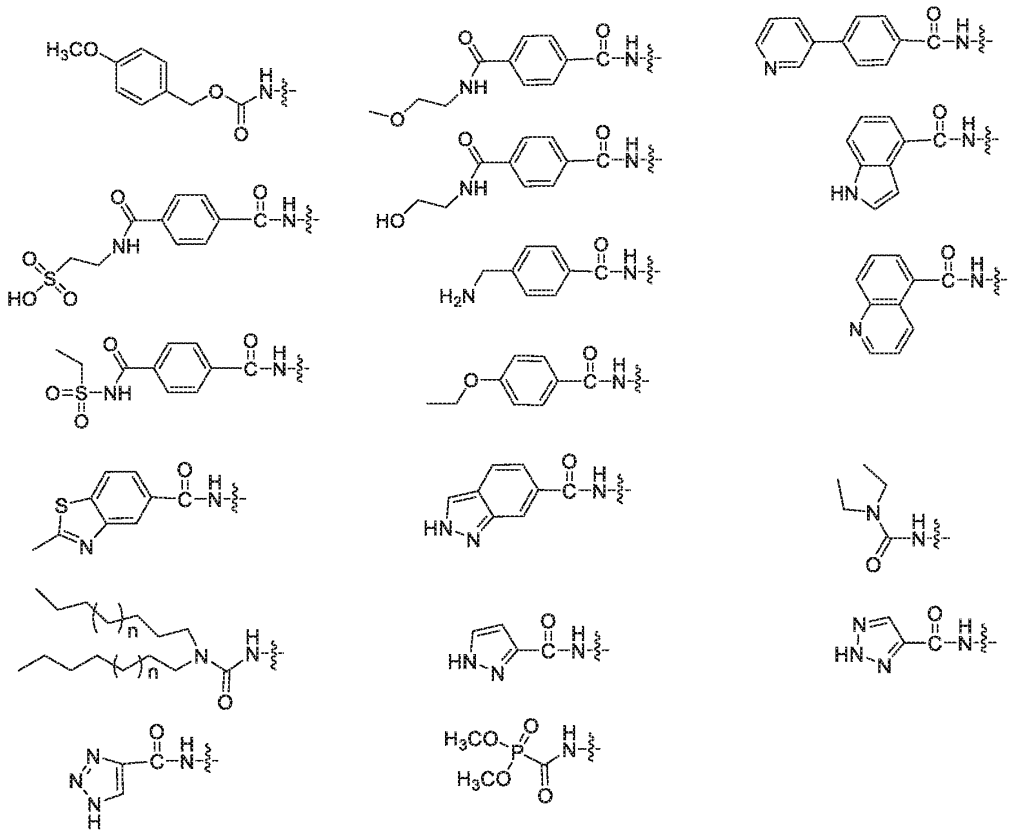
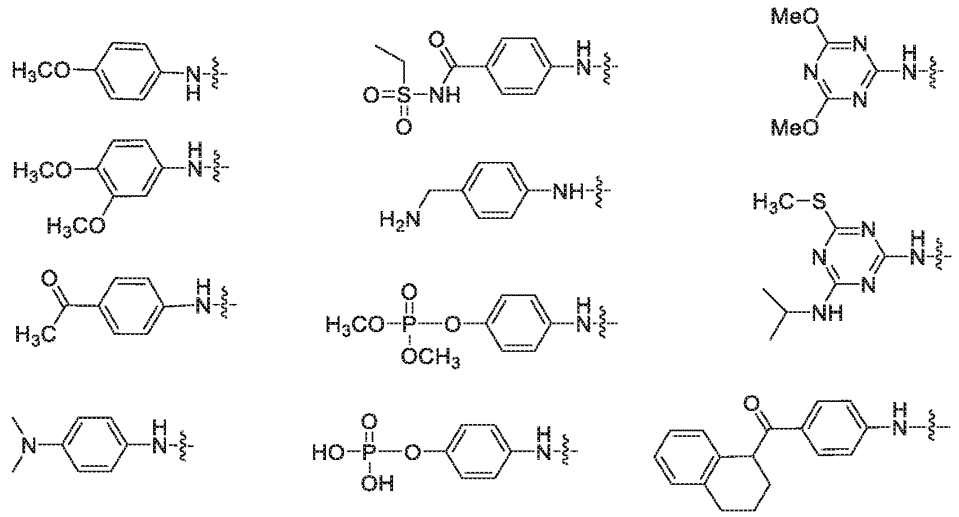
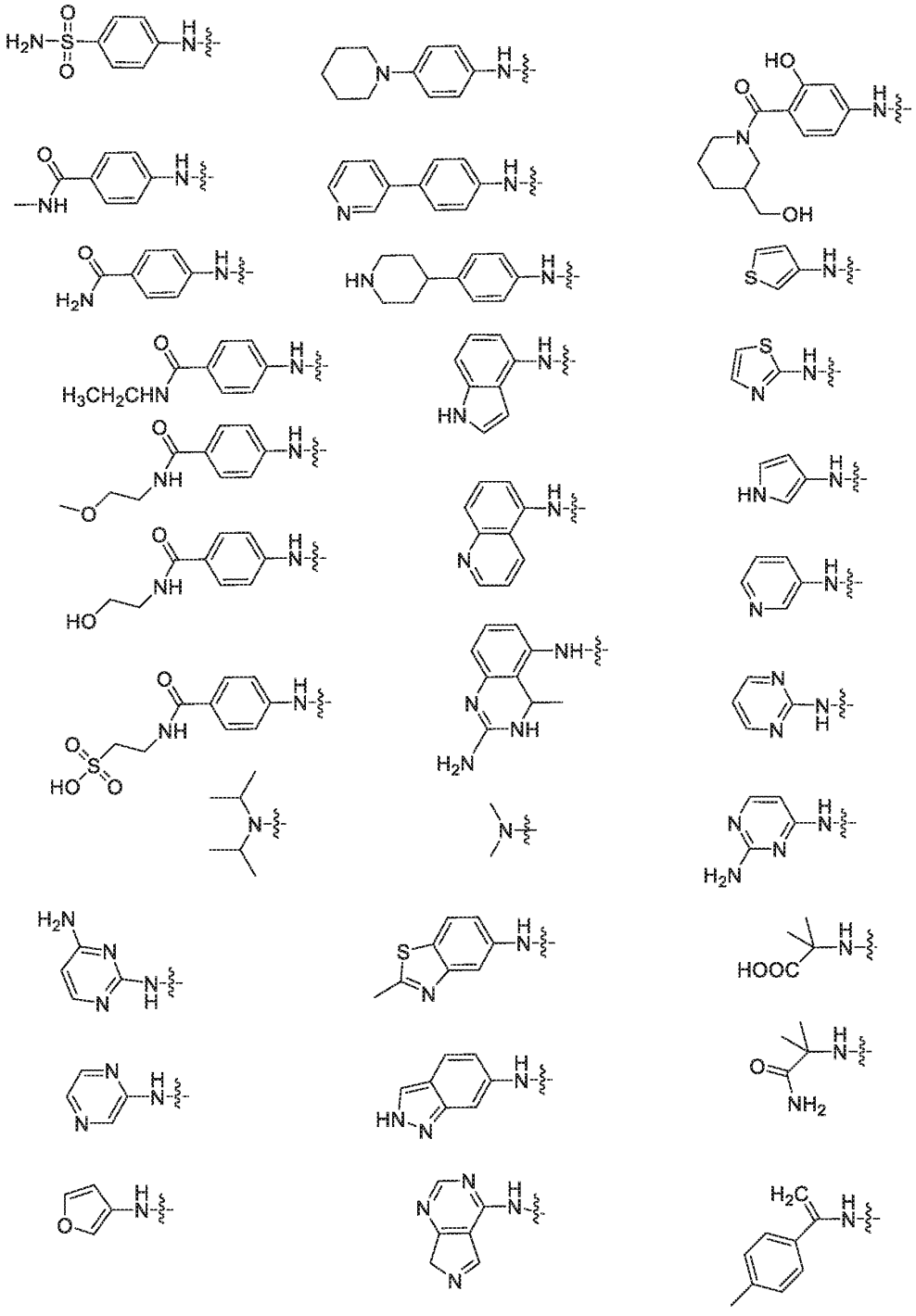


Table L-5. Certain useful moieties bonded to linkage phosphorus (e.g., −X−R^L).





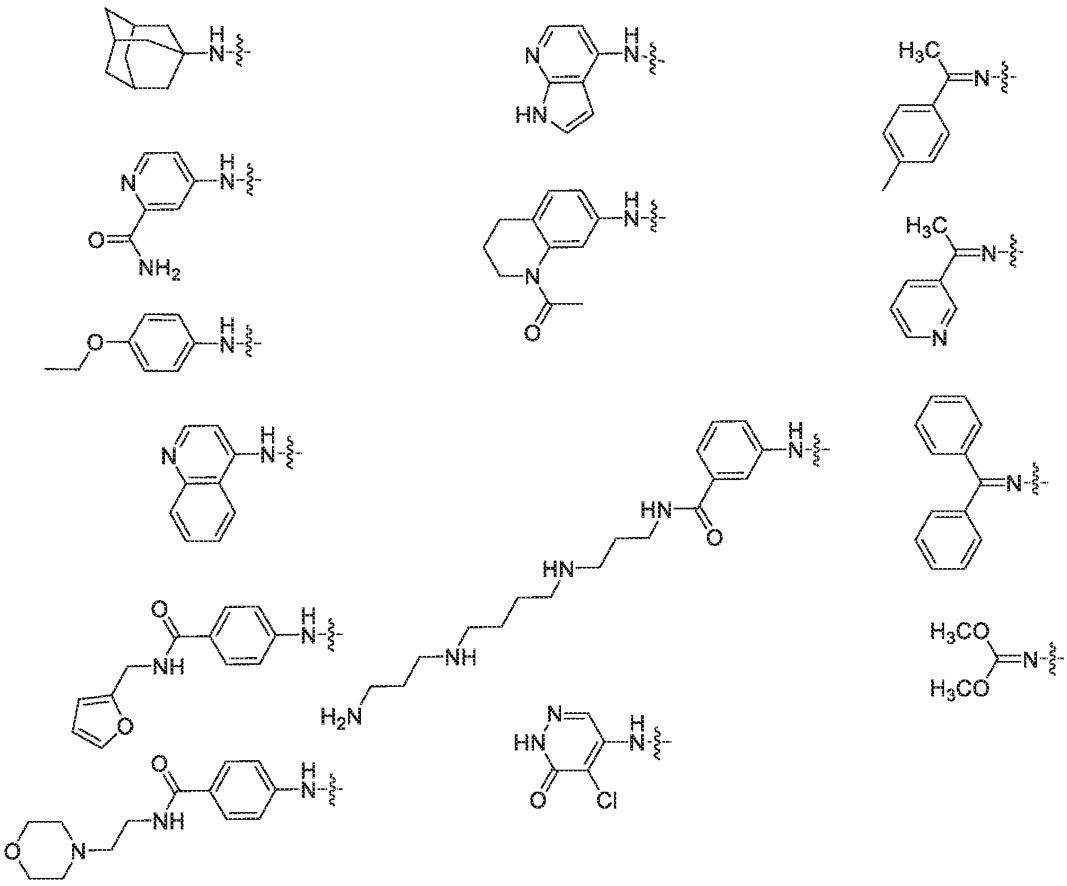
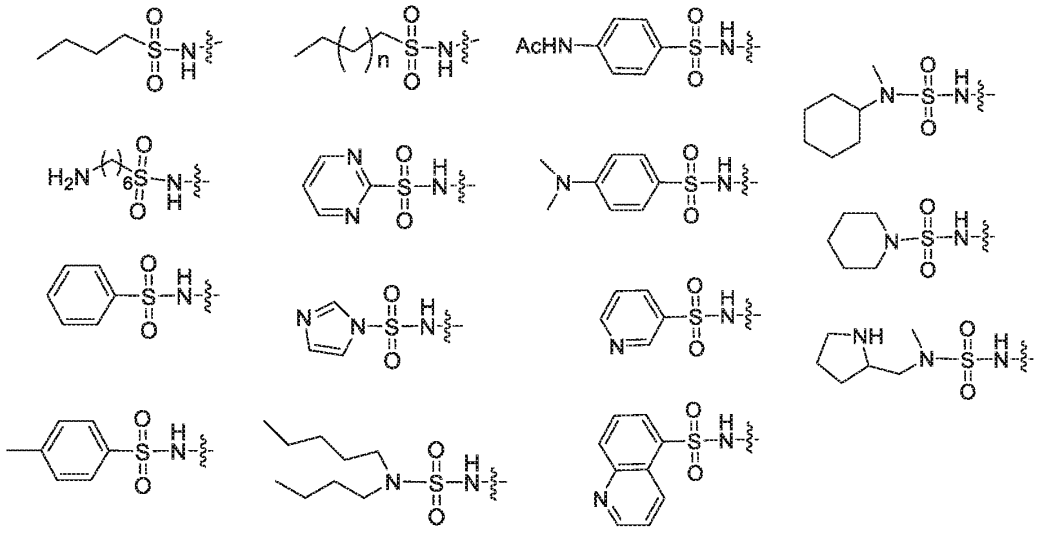
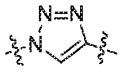
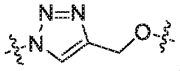


Table L-6. Certain useful moieties bonded to linkage phosphorus (e.g., −X−R^L).



[00879] In some embodiments, an internucleotidic linkage, e.g., an non-negatively charged internucleotidic

linkage or a neutral internucleotidic linkage, has the structure of $-L^{L1}-Cy^{IL}-L^{L2}-$. In some embodiments, L^{L1} is bonded to a 3'-carbon of a sugar. In some embodiments, L^{L2} is bonded to a 5'-carbon of a sugar. In some embodiments, L^{L1} is $-O-CH_2-$. In some embodiments, L^{L2} is a covalent bond. In some embodiments, L^{L2} is a $-N(R')-$. In some embodiments, L^{L2} is a $-NH-$. In some embodiments, L^{L2} is bonded to a 5'-carbon of a sugar, which 5'-carbon is substituted with =O. In some embodiments, Cy^{IL} is optionally substituted 3-10 membered saturated, partially unsaturated, or aromatic ring having 0-5 heteroatoms. In some embodiments, Cy^{IL} is an optionally substituted triazole ring. In some embodiments, Cy^{IL} is . In some embodiments, a linkage is .

[00880] In some embodiments, a non-negatively charged internucleotidic linkage has the structure of $-OP(=W)(-N(R')_2)-O-$.

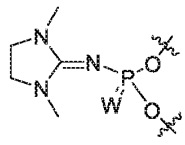
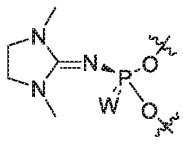
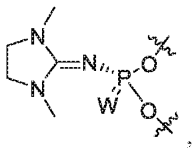
[00881] In some embodiments, R' is R. In some embodiments, R' is $-H$. In some embodiments, R' is $-C(O)R$. In some embodiments, R' is $-C(O)OR$. In some embodiments, R' is $-S(O)_2R$.

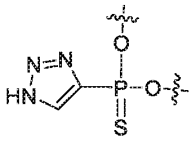
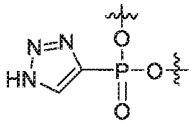
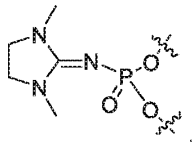
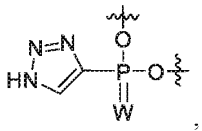
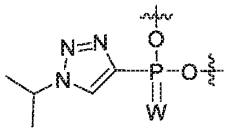
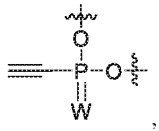
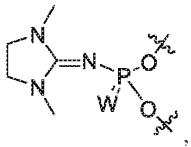
[00882] In some embodiments, R" is $-NHR'$. In some embodiments, $-N(R')_2$ is $-NHR'$.

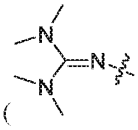
[00883] As described herein, some embodiments, R is $-H$. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is methyl. In some embodiments, R is substituted methyl. In some embodiments, R is ethyl. In some embodiments, R is substituted ethyl.

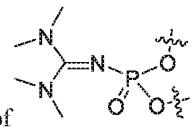
[00884] In some embodiments, as described herein, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage.

[00885] In some embodiments, a modified internucleotidic linkage (e.g., a non-negatively charged internucleotidic linkage) comprises optionally substituted triazolyl. In some embodiments, R' is or comprises optionally substituted triazolyl. In some embodiments, a modified internucleotidic linkage (e.g., a non-negatively charged internucleotidic linkage) comprises optionally substituted alkynyl. In some embodiments, R' is optionally substituted alkynyl. In some embodiments, R' comprises an optionally substituted triple bond. In some embodiments, a modified internucleotidic linkage comprises a triazole or alkyne moiety. In some embodiments, R' is or comprises an optionally substituted triazole or alkyne moiety. In some embodiments, a triazole moiety, e.g., a triazolyl group, is optionally substituted. In some embodiments, a triazole moiety, e.g., a triazolyl group) is substituted. In some embodiments, a triazole moiety is unsubstituted. In some embodiments, a modified internucleotidic linkage comprises an optionally substituted guanidine moiety. In some embodiments, a modified internucleotidic linkage comprises an optionally substituted cyclic guanidine moiety. In some embodiments, R', R^L, or $-X-R^L$, is or comprises an optionally substituted guanidine moiety. In some embodiments, R', R^L, or $-X-R^L$, is or comprises an optionally substituted cyclic guanidine moiety. In some embodiments, R', R^L, or $-X-R^L$ comprises an optionally substituted cyclic guanidine moiety and an

internucleotidic linkage has the structure of: , , or , wherein W is O or S. In some embodiments, W is O. In some embodiments, W is S. In some embodiments, a non-negatively charged internucleotidic linkage is stereochemically controlled.

[00886] In some embodiments, a non-negatively charged internucleotidic linkage or a neutral internucleotidic linkage is an internucleotidic linkage comprising a triazole moiety. In some embodiments, a non-negatively charged internucleotidic linkage or a non-negatively charged internucleotidic linkage comprises an optionally substituted triazolyl group. In some embodiments, an internucleotidic linkage comprising a triazole moiety (e.g., an optionally substituted triazolyl group) has the structure of . In some embodiments, an internucleotidic linkage comprising a triazole moiety has the structure of . In some embodiments, an internucleotidic linkage, e.g., a non-negatively charged internucleotidic linkage, a neutral internucleotidic linkage, comprises a cyclic guanidine moiety. In some embodiments, an internucleotidic linkage comprising a cyclic guanidine moiety has the structure of . In some embodiments, a non-negatively charged internucleotidic linkage, or a neutral internucleotidic linkage, is or comprising a structure selected from , , , , or , wherein W is O or S.

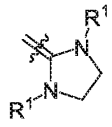
[00887] In some embodiments, an internucleotidic linkage comprises a Tmg group (). In some



embodiments, an internucleotidic linkage comprises a Tmg group and has the structure of (the "Tmg internucleotidic linkage"). In some embodiments, neutral internucleotidic linkages include internucleotidic linkages of PNA and PMO, and an Tmg internucleotidic linkage.

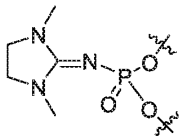
[00888] In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 3-20 membered heterocyclyl or heteroaryl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 3-20 membered heterocyclyl or heteroaryl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, such a heterocyclyl or heteroaryl group is of a 5-membered ring. In some embodiments, such a heterocyclyl or heteroaryl group is of a 6-membered ring.

[00889] In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heteroaryl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heteroaryl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-6 membered heteroaryl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-membered heteroaryl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a heteroaryl group is directly bonded to a linkage phosphorus. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heterocyclyl group having 1-10 heteroatoms. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-20 membered heterocyclyl group having 1-10 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-6 membered heterocyclyl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted 5-membered heterocyclyl group having 1-4 heteroatoms, wherein at least one heteroatom is nitrogen. In some embodiments, at least two heteroatoms are nitrogen. In some embodiments, a heterocyclyl group is directly bonded to a linkage phosphorus. In some embodiments, a heterocyclyl group is bonded to a linkage phosphorus through a linker, e.g., =N– when the heterocyclyl group is part of a guanidine moiety who directed bonded to a linkage phosphorus through its =N–. In some embodiments, a non-negatively charged internucleotidic linkage comprises an optionally substituted  group. In some embodiments, a non-negatively charged

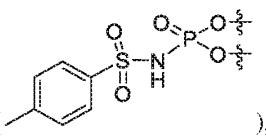
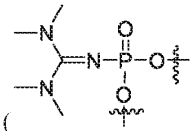
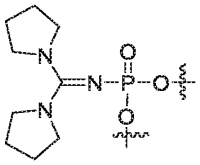
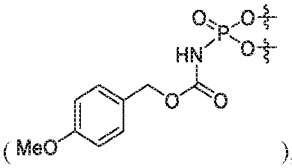
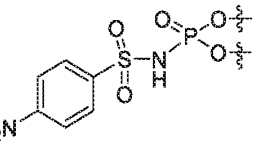
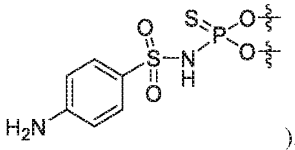
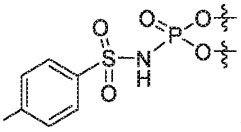
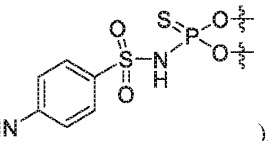
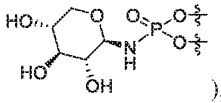
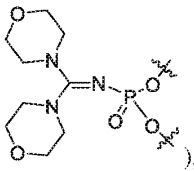
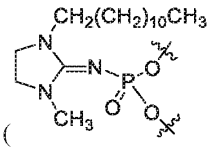
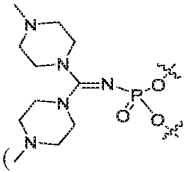
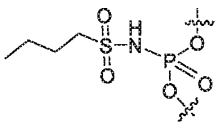
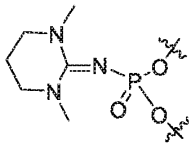
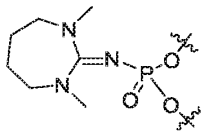
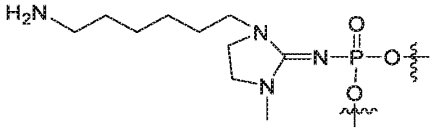
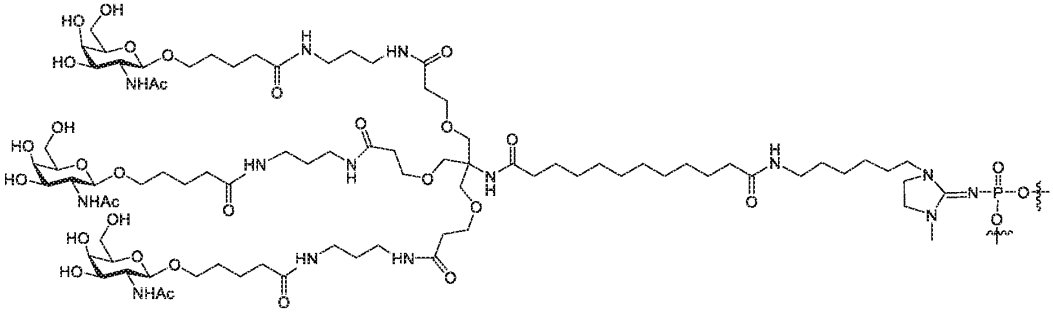
internucleotidic linkage comprises an substituted  group. In some embodiments, a non-negatively charged internucleotidic linkage comprises a  group. In some embodiments, each R^1 is independently optionally substituted C_{1-6} alkyl. In some embodiments, each R^1 is independently methyl.

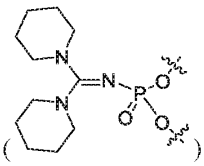
[00890] In some embodiments, a non-negatively charged internucleotidic linkage, e.g., a neutral internucleotidic linkage is not chirally controlled. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled and its linkage phosphorus is Rp. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled and its linkage phosphorus is Sp.

[00891] In some embodiments, an internucleotidic linkage comprises no linkage phosphorus. In some embodiments, an internucleotidic linkage has the structure of −C(O)−(O)− or −C(O)−N(R')−, wherein R' is as described herein. In some embodiments, an internucleotidic linkage has the structure of −C(O)−(O)−. In some embodiments, an internucleotidic linkage has the structure of −C(O)−N(R')−, wherein R' is as described herein. In various embodiments, −C(O)− is bonded to nitrogen. In some embodiments, an internucleotidic linkage is or comprises −C(O)−O− which is part of a carbamate moiety. In some embodiments, an internucleotidic linkage is or comprises −C(O)−O− which is part of a urea moiety.

[00892] In some embodiments, an oligonucleotide comprises 1-20, 1-15, 1-10, 1-5, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more non-negatively charged internucleotidic linkages. In some embodiments, an oligonucleotide comprises 1-20, 1-15, 1-10, 1-5, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or more neutral internucleotidic linkages. In some embodiments, each of non-negatively charged internucleotidic linkage and/or neutral internucleotidic linkages is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage in an oligonucleotide is independently a chirally controlled internucleotidic linkage. In some embodiments, each neutral internucleotidic linkage in an oligonucleotide is independently a chirally controlled internucleotidic linkage. In some embodiments, at least one non-negatively charged internucleotidic linkage/neutral internucleotidic linkage has the structure of . In some embodiments, an oligonucleotide comprises at least one non-negatively charged internucleotidic linkage wherein its linkage phosphorus is in Rp configuration, and at least one non-negatively charged internucleotidic linkage wherein its linkage phosphorus is in Sp configuration.

[00893] In many embodiments, as demonstrated extensively, oligonucleotides of the present disclosure comprise two or more different internucleotidic linkages. In some embodiments, an oligonucleotide comprises

a phosphorothioate internucleotidic linkage and a non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises a phosphorothioate internucleotidic linkage, a non-negatively charged internucleotidic linkage, and a natural phosphate linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001, n002 (), n003 (), n004 (), n005 (), n006-2 (), n006sp-2 (), n006 (), n006sp (), n007 (), n008 (), n009 (), n010 (), or n013. In some embodiments, a non-negatively charged internucleotidic linkage is n020 (), n025 (), n026 (), n051 (), n057 (), or

n078 (). In some embodiments, a non-negatively charged internucleotidic linkage is n001. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, each chiral modified internucleotidic linkage is independently chirally controlled. In some embodiments, one or more non-negatively charged internucleotidic linkage are not chirally controlled.

[00894] A typical connection, as in natural DNA and RNA, is that an internucleotidic linkage forms bonds with two sugars (which can be either unmodified or modified as described herein). In many embodiments, as exemplified herein, an internucleotidic linkage forms bonds through oxygen atoms or heteroatoms with one optionally modified ribose or deoxyribose at its 5' carbon, and the other optionally modified ribose or deoxyribose at its 3' carbon. In some embodiments, internucleotidic linkages connect sugars that are not ribose sugars, e.g., sugars comprising N ring atoms and acyclic sugars as described herein. In some embodiments, linkage phosphorus of an internucleotidic linkage (e.g., a natural phosphate linkage, a phosphorothioate internucleotidic linkage, a PN internucleotidic linkage (e.g., n001, MsPA, etc.)) is bonded to an oxygen atom which is bonded to a carbon atom of a sugar (e.g., a 5'-carbon), and an oxygen atom which is bonded to a carbon atom of a sugar (e.g., a 3'-carbon). See, e.g., various oligonucleotides in Table 1 and Table 1A.

[00895] In some embodiments, each nucleoside units connected by an internucleotidic linkage independently comprises a nucleobase which is independently an optionally substituted A, T, C, G, or U, or an optionally substituted tautomer of A, T, C, G or U.

[00896] In some embodiments, an oligonucleotide comprises a modified internucleotidic linkage (e.g., a modified internucleotidic linkage having the structure of Formula **I**, **I-a**, **I-b**, or **I-c**, **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc., or a salt form thereof) as described in US 9394333, US 9744183, US 9605019, US 9598458, US 9982257, US 10160969, US 10479995, US 2020/0056173, US 2018/0216107, US 2019/0127733, US 10450568, US 2019/0077817, US 2019/0249173, US 2019/0375774, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, and/or WO 2019/032612 the internucleotidic linkages (e.g., those of Formula **I**, **I-a**, **I-b**, or **I-c**, **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc.,) of each of which are independently incorporated herein by reference. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, provided oligonucleotides comprise one or more non-negatively charged internucleotidic linkages. In some embodiments, a non-negatively charged internucleotidic linkage is a positively charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, the present disclosure provides oligonucleotides comprising one or more neutral internucleotidic linkages. In some

embodiments, a non-negatively charged internucleotidic linkage or a neutral internucleotidic linkage (e.g., one of Formula **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc.) is as described in US 9394333, US 9744183, US 9605019, US 9598458, US 9982257, US 10160969, US 10479995, US 2020/0056173, US 2018/0216107, US 2019/0127733, US 10450568, US 2019/0077817, US 2019/0249173, US 2019/0375774, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, and/or WO 2019/032612. In some embodiments, a non-negatively charged internucleotidic linkage or neutral internucleotidic linkage is one of Formula **I-n-1**, **I-n-2**, **I-n-3**, **I-n-4**, **II**, **II-a-1**, **II-a-2**, **II-b-1**, **II-b-2**, **II-c-1**, **II-c-2**, **II-d-1**, **II-d-2**, etc. as described in WO 2018/223056, WO 2019/032607, WO 2019/075357, WO 2019/032607, WO 2019/075357, WO 2019/200185, WO 2019/217784, and/or WO 2019/032612, such internucleotidic linkages of each of which are independently incorporated herein by reference.

[00897] In some embodiments, an oligonucleotide comprises a PS internucleotidic linkage, a PO internucleotidic linkage or a PN internucleotidic linkage. In some embodiments, an oligonucleotide comprises a PS internucleotidic linkage, a PO internucleotidic linkage and a PN internucleotidic linkage. In some embodiments, an oligonucleotide comprises a PS internucleotidic linkage, a PO internucleotidic linkage, a methylphosphonate and a PN internucleotidic linkage. In some embodiments, each internucleotidic linkage in an oligonucleotide is independently a PS internucleotidic linkage, a PO internucleotidic linkage, a methylphosphonate, or a PN internucleotidic linkage. In some embodiments, a PS internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage. In some embodiments, a PO internucleotidic linkage is a natural phosphate linkage. In some embodiments, each PO internucleotidic linkage is independently a natural phosphate linkage. In some embodiments, a PN internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, each PN internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, a PN internucleotidic linkage is n001. In some embodiments, each PN internucleotidic linkage is n001. In some embodiments, a PN internucleotidic linkage is MsPA. In some embodiments, each PS internucleotidic linkage is independently chirally controlled. In some embodiments, each PN internucleotidic linkage is independently chirally controlled. In some embodiments, each chiral linkage phosphorus is independently chirally controlled.

[00898] In some embodiments, an internucleotidic linkage is a natural phosphate linkage, a phosphorothioate internucleotidic linkage, a phosphoryl guanidine linkage (n001), or a MsPA linkage. In some embodiments, an internucleotidic linkage is a natural phosphate linkage, a phosphorothioate internucleotidic linkage, a *N*-(1,3-dimethylimidazolidin-2-ylidene) phosphoramidate linkage, or a MsPA linkage. In some embodiments, each internucleotidic linkage is independently a natural phosphate linkage, a phosphorothioate internucleotidic linkage, a phosphoryl guanidine linkage, or a MsPA linkage. In some embodiments, each internucleotidic linkage is independently a natural phosphate linkage, a phosphorothioate internucleotidic linkage, a *N*-(1,3-dimethylimidazolidin-2-ylidene) phosphoramidate linkage, or a MsPA linkage. In some

embodiments, linkage phosphorus of such an internucleotidic linkage is bonded to an oxygen atom which is bonded to a carbon atom of a sugar (e.g., a 5'-carbon), and an oxygen atom which is bonded to a carbon atom of a sugar (e.g., a 3'-carbon). See, e.g., various oligonucleotides in Table 1 and Table 1A.

[00899] As described herein, various variables can be R, e.g., R', R^L, etc. Various embodiments for R are described in the present disclosure (e.g., when describing variables that can be R). Such embodiments are generally useful for all variables that can be R. In some embodiments, R is hydrogen. In some embodiments, R is optionally substituted C_{1-30} (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) aliphatic. In some embodiments, R is optionally substituted C_{1-20} aliphatic. In some embodiments, R is optionally substituted C_{1-10} aliphatic. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is optionally substituted alkyl. In some embodiments, R is optionally substituted C_{1-6} alkyl. In some embodiments, R is optionally substituted methyl. In some embodiments, R is methyl. In some embodiments, R is optionally substituted ethyl. In some embodiments, R is optionally substituted propyl. In some embodiments, R is isopropyl. In some embodiments, R is optionally substituted butyl. In some embodiments, R is optionally substituted pentyl. In some embodiments, R is optionally substituted hexyl.

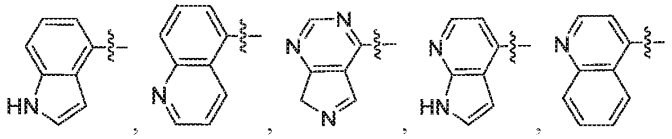
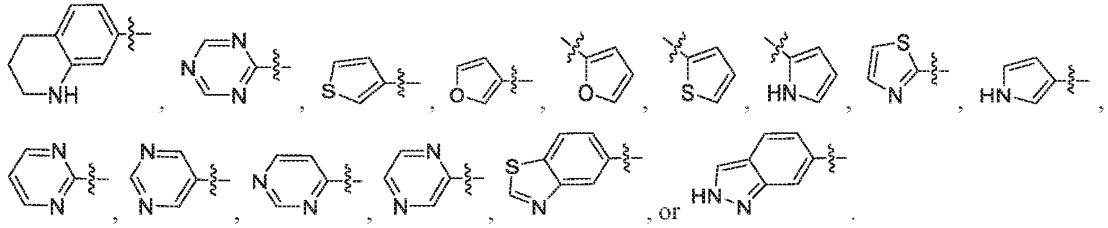
[00900] In some embodiments, R is optionally substituted 3-30 membered (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) cycloaliphatic. In some embodiments, R is optionally substituted cycloalkyl. In some embodiments, cycloaliphatic is monocyclic, bicyclic, or polycyclic, wherein each monocyclic unit is independently saturated or partially saturated. In some embodiments, R is optionally substituted cyclopropyl. In some embodiments, R is optionally substituted cyclobutyl. In some embodiments, R is optionally substituted cyclopentyl. In some embodiments, R is optionally substituted cyclohexyl. In some embodiments, R is optionally substituted adamantyl.

[00901] In some embodiments, R is optionally substituted C_{1-30} (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) heteroaliphatic having 1-10 heteroatoms. In some embodiments, R is optionally substituted C_{1-20} aliphatic having 1-10 heteroatoms. In some embodiments, R is optionally substituted C_{1-10} aliphatic having 1-10 heteroatoms. In some embodiments, R is optionally substituted C_{1-6} aliphatic having 1-3 heteroatoms. In some embodiments, R is optionally substituted heteroalkyl. In some embodiments, R is optionally substituted C_{1-6} heteroalkyl. In some embodiments, R is optionally substituted 3-30 membered (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) heterocycloaliphatic having 1-10 heteroatoms. In some embodiments, R is optionally substituted heteroclycloalkyl. In some embodiments, heterocycloaliphatic is monocyclic, bicyclic, or polycyclic, wherein each monocyclic unit is independently saturated or partially saturated.

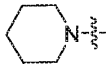
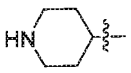
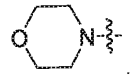
[00902] In some embodiments, R is optionally substituted C_{6-30} aryl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is C_{6-14} aryl. In some embodiments, R is optionally substituted bicyclic aryl. In some embodiments, R is optionally substituted polycyclic aryl. In some embodiments, R is optionally substituted C_{6-30} arylaliphatic. In some

embodiments, R is C_{6-30} arylheteroaliphatic having 1-10 heteroatoms.

[00903] In some embodiments, R is optionally substituted 5-30 (5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) membered heteroaryl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-20 membered heteroaryl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-10 membered heteroaryl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having 1-5 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having 1-3 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 5-membered heteroaryl having one heteroatom. In some embodiments, R is optionally substituted 6-membered heteroaryl having 1-5 heteroatoms. In some embodiments, R is optionally substituted 6-membered heteroaryl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 6-membered heteroaryl having 1-3 heteroatoms. In some embodiments, R is optionally substituted 6-membered heteroaryl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 6-membered heteroaryl having one heteroatom. In some embodiments, R is optionally substituted monocyclic heteroaryl. In some embodiments, R is optionally substituted bicyclic heteroaryl. In some embodiments, R is optionally substituted polycyclic heteroaryl. In some embodiments, a heteroatom is nitrogen.

[00904] In some embodiments, R is optionally substituted 2-pyridinyl. In some embodiments, R is optionally substituted 3-pyridinyl. In some embodiments, R is optionally substituted 4-pyridinyl. In some embodiments, R is optionally substituted , , or .

[00905] In some embodiments, R is optionally substituted 3-30 (3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) membered heterocyclyl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 3-membered heterocyclyl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 4-membered heterocyclyl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 5-20 membered heterocyclyl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-10 membered heterocyclyl having 1-10 heteroatoms. In some embodiments, R is optionally substituted 5-membered heterocyclyl having 1-5 heteroatoms. In some

embodiments, R is optionally substituted 5-membered heterocyclyl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 5-membered heterocyclyl having 1-3 heteroatoms. In some embodiments, R is optionally substituted 5-membered heterocyclyl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 5-membered heterocyclyl having one heteroatom. In some embodiments, R is optionally substituted 6-membered heterocyclyl having 1-5 heteroatoms. In some embodiments, R is optionally substituted 6-membered heterocyclyl having 1-4 heteroatoms. In some embodiments, R is optionally substituted 6-membered heterocyclyl having 1-3 heteroatoms. In some embodiments, R is optionally substituted 6-membered heterocyclyl having 1-2 heteroatoms. In some embodiments, R is optionally substituted 6-membered heterocyclyl having one heteroatom. In some embodiments, R is optionally substituted monocyclic heterocyclyl. In some embodiments, R is optionally substituted bicyclic heterocyclyl. In some embodiments, R is optionally substituted polycyclic heterocyclyl. In some embodiments, R is optionally substituted saturated heterocyclyl. In some embodiments, R is optionally substituted partially unsaturated heterocyclyl. In some embodiments, a heteroatom is nitrogen. In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted . In some embodiments, R is optionally substituted .

[00906] In some embodiments, two R groups are optionally and independently taken together to form a covalent bond. In some embodiments, two or more R groups on the same atom are optionally and independently taken together with the atom to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the atom, 0-10 heteroatoms. In some embodiments, two or more R groups on two or more atoms are optionally and independently taken together with their intervening atoms to form an optionally substituted, 3-30 membered, monocyclic, bicyclic or polycyclic ring having, in addition to the intervening atoms, 0-10 heteroatoms.

[00907] Various variables may comprises an optionally substituted ring, or can be taken together with their intervening atom(s) to form a ring. In some embodiments, a ring is 3-30 (e.g., 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) membered. In some embodiments, a ring is 3-20 membered. In some embodiments, a ring is 3-15 membered. In some embodiments, a ring is 3-10 membered. In some embodiments, a ring is 3-8 membered. In some embodiments, a ring is 3-7 membered. In some embodiments, a ring is 3-6 membered. In some embodiments, a ring is 4-20 membered. In some embodiments, a ring is 5-20 membered. In some embodiments, a ring is monocyclic. In some embodiments, a ring is bicyclic. In some embodiments, a ring is polycyclic. In some embodiments, each monocyclic ring or each monocyclic ring unit in bicyclic or polycyclic rings is independently saturated, partially saturated or aromatic. In some embodiments, each monocyclic ring or each monocyclic ring unit in bicyclic or polycyclic rings is independently 3-10 membered and has 0-5 heteroatoms.

[00908] In some embodiments, each heteroatom is independently selected oxygen, nitrogen, sulfur, silicon, and phosphorus. In some embodiments, each heteroatom is independently selected oxygen, nitrogen, sulfur, and phosphorus. In some embodiments, each heteroatom is independently selected oxygen, nitrogen, and sulfur. In some embodiments, a heteroatom is in an oxidized form.

[00909] As described herein, various groups may be optionally substituted. Substituents are routinely utilized in chemistry including in development of various therapeutics. Many substituents can be utilized in accordance with the present disclosure. In some embodiments, an optionally substituted group is unsubstituted. In some embodiments, an optionally substituted group is substituted. Substituents are preferably those that result in the formation of compounds (e.g., oligonucleotides, reagents, etc.) for a desired property, activity, use, etc., as described herein. In some embodiments, compounds are stable for therapeutic use as described herein. The term "stable," as used herein, refers to oligonucleotides, agents, etc. that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein. In some embodiments, a substituent is a hydrocarbon group. In some embodiments, a substituent comprises a heteroatom. In some embodiments, a substituent comprises multiple heteroatoms. In some embodiments, each atom in a substituent is independently selected from hydrogen, carbon, halogen, nitrogen, oxygen, sulfur, phosphorus and silicon. In some embodiments, each atom in a substituent is independently selected from hydrogen, carbon, halogen, nitrogen, oxygen, and sulfur. In some embodiments, each atom in a substituent is independently selected from hydrogen, carbon, fluorine, chlorine, bromine, iodine, nitrogen, oxygen, and sulfur. In some embodiments, the total number of carbon and non-halogen heteroatom(s) in a substituent is about or no more than about 1; in some embodiments, it is no more than about 2; in some embodiments, it is no more than about 3; in some embodiments, it is no more than about 4; in some embodiments, it is no more than about 5; in some embodiments, it is no more than about 6; in some embodiments, it is no more than about 7; in some embodiments, it is no more than about 8; in some embodiments, it is no more than about 9; in some embodiments, it is no more than about 10; in some embodiments, it is no more than about 11; in some embodiments, it is no more than about 12; in some embodiments, it is no more than about 13; in some embodiments, it is no more than about 14; in some embodiments, it is no more than about 15; in some embodiments, it is no more than about 20. In some embodiments, the total number of carbon and non-halogen heteroatom(s) in each substituent is independently no more than about 20. In some embodiments, the total number of carbon and non-halogen heteroatom(s) in each substituent is independently no more than about 15. In some embodiments, the total number of carbon and non-halogen heteroatom(s) in each substituent is independently no more than about 10. In some embodiments, the total number of carbon and non-halogen heteroatom(s) in each substituent is independently no more than about 6.

[00910] As appreciated by those skilled in the art, many other types of internucleotidic linkages may be utilized in accordance with the present disclosure, for example, those described in U.S. Pat. Nos. 3,687,808; 4,469,863; 4,476,301; 5,177,195; 5,023,243; 5,034,506; 5,166,315; 5,185,444; 5,188,897; 5,214,134;

5,216,141; 5,235,033; 5,264,423; 5,264,564; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,938; 5,405,939; 5,434,257; 5,453,496; 5,455,233; 5,466,677; 5,466,677; 5,470,967; 5,476,925; 5,489,677; 5,519,126; 5,536,821; 5,541,307; 5,541,316; 5,550,111; 5,561,225; 5,563,253; 5,571,799; 5,587,361; 5,596,086; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,625,050; 5,633,360; 5,64,562; 5,663,312; 5,677,437; 5,677,439; 6,160,109; 6,239,265; 6,028,188; 6,124,445; 6,169,170; 6,172,209; 6,277,603; 6,326,199; 6,346,614; 6,444,423; 6,531,590; 6,534,639; 6,608,035; 6,683,167; 6,858,715; 6,867,294; 6,878,805; 7,015,315; 7,041,816; 7,273,933; 7,321,029; or RE39464. In some embodiments, a modified internucleotidic linkage is one described in US 9394333, US 9744183, US 9605019, US 9598458, US 9982257, US 10160969, US 10479995, US 2020/0056173, US 2018/0216107, US 2019/0127733, US 10450568, US 2019/0077817, US 2019/0249173, US 2019/0375774, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, and/or WO 2019/032612, the nucleobases, sugars, internucleotidic linkages, chiral auxiliaries/reagents, and technologies for oligonucleotide synthesis (reagents, conditions, cycles, etc.) of each of which is independently incorporated herein by reference.

[00911] In some embodiments, each internucleotidic linkage in an oligonucleotide is independently selected from a natural phosphate linkage, a phosphorothioate linkage, and a non-negatively charged internucleotidic linkage (e.g., n001, n002, n003, n004, n005, n006, n007, n008, n009, n010, n013, etc.). In some embodiments, each internucleotidic linkage in an oligonucleotide is independently selected from a natural phosphate linkage, a phosphorothioate linkage, and a neutral internucleotidic linkage (e.g., n001, n002, n003, n004, n005, n006, n007, n008, n009, n010, n013, etc.).

[00912] Oligonucleotides can comprise various numbers of natural phosphate linkages, e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1-10, 1-5, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more. In some embodiments, one or more (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 1-10, 1-5, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) of the natural phosphate linkages in an oligonucleotide are consecutive. In some embodiments, provided oligonucleotides comprise no natural phosphate linkages. In some embodiments, provided oligonucleotides comprise one natural phosphate linkage. In some embodiments, provided oligonucleotides comprise 1 to 30 or more natural phosphate linkages.

[00913] In some embodiments, a modified internucleotidic linkage is a chiral internucleotidic linkage which comprises a chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is a phosphorothioate linkage. In some embodiments, a chiral internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a chiral internucleotidic linkage is chirally controlled with respect to its chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is stereochemically pure with respect to its chiral linkage phosphorus. In some embodiments, a chiral internucleotidic linkage is not chirally controlled. In some embodiments, a pattern of backbone chiral centers comprises or consists of positions and linkage phosphorus configurations of chirally controlled internucleotidic linkages (*R*p or *S*p) and positions of

achiral internucleotidic linkages (e.g., natural phosphate linkages).

[00914] In some embodiments, provided oligonucleotides comprise one or more non-negatively charged internucleotidic linkages. In some embodiments, provided oligonucleotides comprise one or more neutral internucleotidic linkages. In some embodiments, provided oligonucleotides comprise one or more phosphoryl guanidine internucleotidic linkages. In some embodiments, a neutral internucleotidic linkage or non-negatively charged internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, each neutral internucleotidic linkage or non-negatively charged internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, each neutral internucleotidic linkage and non-negatively charged internucleotidic linkage is independently n001.

[00915] In some embodiments, each internucleotidic linkage in a provided oligonucleotide is independently selected from a phosphorothioate internucleotidic linkage, a phosphoryl guanidine internucleotidic linkage, and a natural phosphate linkage. In some embodiments, each internucleotidic linkage in a provided oligonucleotide is independently selected from a phosphorothioate internucleotidic linkage, n001, n006, and a natural phosphate linkage. In some embodiments, each internucleotidic linkage in a provided oligonucleotide is independently selected from a phosphorothioate internucleotidic linkage, n001, and a natural phosphate linkage.

[00916] Various types of internucleotidic linkages may be utilized in combination of other structural elements, e.g., sugars, to achieve desired oligonucleotide properties and/or activities. For example, the present disclosure routinely utilizes modified internucleotidic linkages and modified sugars, optionally with natural phosphate linkages and natural sugars, in designed oligonucleotides. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars and one or more modified internucleotidic linkages, one or more of which are natural phosphate linkages.

[00917] In some embodiments, an internucleotidic linkage is a phosphoryl guanidine, phosphoryl amidine, phosphoryl isourea, phosphoryl isothiourea, phosphoryl imidate, or phosphoryl imidothioate internucleotidic linkage, e.g., those as described in US 20170362270.

[00918] As appreciated by those skilled in the art, many other types of internucleotidic linkages may be utilized in accordance with the present disclosure, for example, those described in U.S. Pat. Nos. 3,687,808; 4,469,863; 4,476,301; 5,177,195; 5,023,243; 5,034,506; 5,166,315; 5,185,444; 5,188,897; 5,214,134; 5,216,141; 5,235,033; 5,264,423; 5,264,564; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,938; 5,405,939; 5,434,257; 5,453,496; 5,455,233; 5,466,677; 5,466,677; 5,470,967; 5,476,925; 5,489,677; 5,519,126; 5,536,821; 5,541,307; 5,541,316; 5,550,111; 5,561,225; 5,563,253; 5,571,799; 5,587,361; 5,596,086; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,625,050; 5,633,360; 5,64,562; 5,663,312; 5,677,437; 5,677,439; 6,160,109; 6,239,265; 6,028,188; 6,124,445; 6,169,170; 6,172,209; 6,277,603; 6,326,199; 6,346,614; 6,444,423; 6,531,590; 6,534,639; 6,608,035; 6,683,167; 6,858,715; 6,867,294; 6,878,805; 7,015,315; 7,041,816; 7,273,933; 7,321,029; or RE39464. In some

embodiments, a modified internucleotidic linkage is one described in US 9982257, US 20170037399, US 20180216108, WO 2017192664, WO 2017015575, WO 2017062862, WO 2018067973, WO 2017160741, WO 2017192679, WO 2017210647, WO 2018098264, WO 2018223056, WO 2018237194, or WO 2019055951, the nucleobases, sugars, internucleotidic linkages, chiral auxiliaries/reagents, and technologies for oligonucleotide synthesis (reagents, conditions, cycles, etc.) of each of which is independently incorporated herein by reference. In some embodiments, an internucleotidic linkage is described in WO 2012/030683, WO 2021/030778, WO 2019112485, US 20170362270, WO 2018156056, WO 2018056871, WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, or WO 2020/252376, and can be utilized in accordance with the present disclosure.

[00919] In some embodiments, each internucleotidic linkage in an oligonucleotide is independently selected from a natural phosphate linkage, a phosphorothioate linkage, and a non-negatively charged internucleotidic linkage (e.g., n001). In some embodiments, each internucleotidic linkage in an oligonucleotide is independently selected from a natural phosphate linkage, a phosphorothioate linkage, and a neutral internucleotidic linkage (e.g., n001).

[00920] In some embodiments, an oligonucleotide comprises one or more nucleotides that independently comprise a phosphorus modification prone to "autorelease" under certain conditions. That is, under certain conditions, a particular phosphorus modification is designed such that it self-cleaves from the oligonucleotide to provide, e.g., a natural phosphate linkage. In some embodiments, such a phosphorus modification has a structure of –O–L–R^1, wherein L is L^B as described herein, and R^1 is R' as described herein. In some embodiments, a phosphorus modification has a structure of –S–L–R^1, wherein each L and R^1 is independently as described in the present disclosure. Certain examples of such phosphorus modification groups can be found in US 9982257. In some embodiments, an autorelease group comprises a morpholino group. In some embodiments, an autorelease group is characterized by the ability to deliver an agent to the internucleotidic phosphorus linker, which agent facilitates further modification of the phosphorus atom such as, e.g., desulfurization. In some embodiments, the agent is water and the further modification is hydrolysis to form a natural phosphate linkage.

[00921] In some embodiments, an oligonucleotide comprises one or more internucleotidic linkages that improve one or more pharmaceutical properties and/or activities of the oligonucleotide. It is well documented in the art that certain oligonucleotides are rapidly degraded by nucleases and exhibit poor cellular uptake through the cytoplasmic cell membrane (Poijarvi-Virta et al., Curr. Med. Chem. (2006), 13(28);3441-65; Wagner et al., Med. Res. Rev. (2000), 20(6):417-51; Peyrottes et al., Mini Rev. Med. Chem. (2004), 4(4):395-408; Gosselin et al., (1996), 43(1):196-208; Bologna et al., (2002), Antisense & Nucleic Acid Drug Development 12:33-41). Vives et al. (Nucleic Acids Research (1999), 27(20):4071-76) reported that tert-butyl SATE pro-oligonucleotides displayed markedly increased cellular penetration compared to the parent oligonucleotide under certain conditions.

[00922] Oligonucleotides can comprise various number of natural phosphate linkages. In some

embodiments, 5% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 10% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 15% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 20% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 25% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 30% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 35% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, 40% or more of the internucleotidic linkages of provided oligonucleotides are natural phosphate linkages. In some embodiments, provided oligonucleotides comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more natural phosphate linkages. In some embodiments, provided oligonucleotides comprises 4, 5, 6, 7, 8, 9, 10 or more natural phosphate linkages. In some embodiments, the number of natural phosphate linkages is 2. In some embodiments, the number of natural phosphate linkages is 3. In some embodiments, the number of natural phosphate linkages is 4. In some embodiments, the number of natural phosphate linkages is 5. In some embodiments, the number of natural phosphate linkages is 6. In some embodiments, the number of natural phosphate linkages is 7. In some embodiments, the number of natural phosphate linkages is 8. In some embodiments, some or all of the natural phosphate linkages are consecutive. In some embodiments, no more than a certain number of internucleotidic linkages of the provided oligonucleotides are natural phosphate linkages, e.g., no more than 1, no more than 2, no more than 3, no more than 4, no more than 5, no more than 6, no more than 7, no more than 8, no more than 9, no more than 10, no more than 11, no more than 12, no more than 13, no more than 14, no more than 15, no more than 16, no more than 17, no more than 18, no more than 19, no more than 20, no more than 21, no more than 22, no more than 23, no more than 24, no more than 25, no more than 26, no more than 27, no more than 28, no more than 29, or no more than 30 natural phosphate linkages. In some embodiments, provided oligonucleotides comprise no natural phosphate linkages.

[00923] In some embodiments, the present disclosure demonstrates that, in at least some cases, *Sp* internucleotidic linkages, among other things, at the 5'- and/or 3'-end can improve oligonucleotide stability. In some embodiments, the present disclosure demonstrates that, among other things, natural phosphate linkages and/or *Rp* internucleotidic linkages may improve removal of oligonucleotides from a system. As appreciated by a person having ordinary skill in the art, various assays known in the art can be utilized to assess such properties in accordance with the present disclosure.

[00924] In some embodiments, each phosphorothioate internucleotidic linkage in an oligonucleotide or a portion thereof (e.g., a domain, a subdomain, etc.) is independently chirally controlled. In some embodiments, each is independently *Sp* or *Rp*. In some embodiments, a high level is *Sp* as described herein. In some embodiments, each phosphorothioate internucleotidic linkage in an oligonucleotide or a portion thereof is chirally controlled and is *Sp*. In some embodiments, one or more, e.g., about 1-5 (e.g., about 1, 2, 3, 4, or 5)

is *R*p.

[00925] In some embodiments, as illustrated in certain examples, an oligonucleotide or a portion thereof comprises one or more non-negatively charged internucleotidic linkages, each of which is optionally and independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, each chiral non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *R*p. In some embodiments, a chiral non-negatively charged internucleotidic linkage is chirally controlled and is *S*p. In some embodiments, each chiral non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, the number of non-negatively charged internucleotidic linkages in an oligonucleotide or a portion thereof is about 1-10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, it is about 1. In some embodiments, it is about 2. In some embodiments, it is about 3. In some embodiments, it is about 4. In some embodiments, it is about 5. In some embodiments, it is about 6. In some embodiments, it is about 7. In some embodiments, it is about 8. In some embodiments, it is about 9. In some embodiments, it is about 10. In some embodiments, two or more non-negatively charged internucleotidic linkages are consecutive. In some embodiments, no two non-negatively charged internucleotidic linkages are consecutive. In some embodiments, all non-negatively charged internucleotidic linkages in an oligonucleotide or a portion thereof are consecutive (e.g., 3 consecutive non-negatively charged internucleotidic linkages). In some embodiments, a non-negatively charged internucleotidic linkage, or two or more (e.g., about 2, about 3, about 4 etc.) consecutive non-negatively charged internucleotidic linkages, are at the 3'-end of an oligonucleotide or a portion thereof. In some embodiments, the last two or three or four internucleotidic linkages of an oligonucleotide or a portion thereof comprise at least one internucleotidic linkage that is not a non-negatively charged internucleotidic linkage. In some embodiments, the last two or three or four internucleotidic linkages of an oligonucleotide or a portion thereof comprise at least one internucleotidic linkage that is not n001. In some embodiments, the internucleotidic linkage linking the first two nucleosides of an oligonucleotide or a portion thereof is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the last two nucleosides of an oligonucleotide or a portion thereof is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage linking the first two nucleosides of an oligonucleotide or a portion thereof is a phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p. In some embodiments, the internucleotidic linkage linking the last two nucleosides of an oligonucleotide or a portion thereof is a phosphorothioate internucleotidic linkage. In some embodiments, it is *S*p.

[00926] In some embodiments, one or more chiral internucleotidic linkages are chirally controlled and one or more chiral internucleotidic linkages are not chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled, and one or more non-negatively

charged internucleotidic linkage are not chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled, and each non-negatively charged internucleotidic linkage is not chirally controlled. In some embodiments, the internucleotidic linkage between the first two nucleosides of an oligonucleotide is a non-negatively charged internucleotidic linkage. In some embodiments, the internucleotidic linkage between the last two nucleosides are each independently a non-negatively charged internucleotidic linkage. In some embodiments, both are independently non-negatively charged internucleotidic linkages. In some embodiments, an oligonucleotide comprises one or more additional internucleotidic linkages, e.g., one of which is between the nucleosides at positions -1 and -2 relative to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) (the two nucleosides immediately 3' to a nucleoside opposite to a target nucleoside (e.g., in $\ldots N_0N_{-1}N_{-2}\ldots$, N_0 is a nucleoside opposite to a target nucleoside, N_{-1} and N_{-2} are at positions -1 and -2, respectively). In some embodiments, each non-negatively charged internucleotidic linkage is independently neutral internucleotidic linkage. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001.

[00927] As demonstrated herein, in some embodiments, non-negatively charged internucleotidic linkages such as n001 may provide improved properties and/or activities. In some embodiments, in an oligonucleotide a 5'-end internucleotidic linkage and/or a 3'-end internucleotidic linkage, each of which is independently bonded to two nucleosides comprising a nucleobase as described herein, is a non-negatively charged internucleotidic linkage as described herein. In some embodiments, the first one or more (e.g., the first 1, 2, and/or 3), and/or the last one or more (e.g., the last 1, 2, 3, 4, 5, 6 or 7) internucleotidic linkages, each of which is independently bonded to two nucleosides in a first domain, is independently a non-negatively charged internucleotidic linkage. In some embodiments, the first internucleotidic linkage of a first domain is a non-negatively charged internucleotidic linkage. In some embodiments, the last internucleotidic linkage that bonds to two nucleosides of a first domain is a non-negatively charged internucleotidic linkage. In some embodiments, the last internucleotidic linkage of a second domain is a non-negatively charged internucleotidic linkage. In some embodiments, one or more of internucleotidic linkages in the middle of a second domain, e.g., one or more of the 4th, 5th and 6th internucleotidic linkages, each of which independently bonds to two nucleosides of a second domain, is independently a non-negatively charged internucleotidic linkage. In some embodiments, the 11th internucleotidic linkage that bonds to two nucleosides of a second domain is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage that is not bonded to a nucleoside opposite to a target nucleoside but is bonded to its 3' immediate nucleoside is a non-negatively charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001. In some embodiments, each non-negatively charged internucleotidic linkage is n001. In some embodiments, a non-negatively charged internucleotidic linkage is stereorandom. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled and is *Rp*. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled and is *Sp*. In some embodiments, each non-

negatively charged internucleotidic linkage is independently chirally controlled. In some embodiments, one or more internucleotidic linkages of a first domain, e.g., one or more of the 4th, 5th, 6th, 7th and 8th internucleotidic linkages each of which is independently bonded to two nucleosides of a first domain, is independently not a non-negatively charged internucleotidic linkage. In some embodiments, one or more internucleotidic linkages of a second domain, e.g., one or more of the 1st, 2nd, 3rd, 7th, 8th, 9th, 12th and 13th internucleotidic linkages each of which is independently bonded to two nucleosides of a first domain, is independently not a non-negatively charged internucleotidic linkage. In some embodiments, one or both of the 2nd and the 3rd internucleotidic linkages of a second domain is not a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage that is not a non-negatively charged internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, it is a stereorandom phosphorothioate internucleotidic linkage. In some embodiments, it is a *Rp* chirally controlled phosphorothioate internucleotidic linkage. In some embodiments, it is a *Sp* chirally controlled phosphorothioate internucleotidic linkage.

[00928] In some embodiments, one or more or all internucleotidic linkages at positions +11, +9, +5, -2, and -5 of a nucleoside opposite to a target adenosine are independently PN internucleotidic linkages, e.g., non-negatively charged internucleotidic linkages ("+" is counting from a nucleoside opposite to a target adenosine toward the 5'-end of an oligonucleotide with the internucleotidic linkage at the +1 position being the internucleotidic linkage between a nucleoside opposite to a target adenosine and its 5' side neighboring nucleoside (e.g., being between N_1 and N_0 of 5'-$N_1N_0N_{-1}$-3', wherein as described herein N_0 is a nucleoside opposite to a target adenosine), and "-" is counting from the nucleoside toward the 3'-end of an oligonucleotide with the internucleotidic linkage at the -1 position being the internucleotidic linkage between a nucleoside opposite to a target adenosine and its 3' side neighboring nucleoside (e.g., being between N_{-1} and N_0 of 5'-$N_1N_0N_{-1}$-3', wherein as described herein N_0 is the nucleoside opposite to a target adenosine)). In some embodiments, the first internucleotidic linkage of an oligonucleotide is a non-negatively charged internucleotidic linkage. In some embodiments, the last internucleotidic linkage of an oligonucleotide is a non-negatively charged internucleotidic linkage. In some embodiments, the first and last internucleotidic linkages of an oligonucleotide are each independently a non-negatively charged internucleotidic linkage. In some embodiments, one or more or all internucleotidic linkages at positions +21, +20, +18, +17, +16, +15, +14, +13, +12, +11, +10, +6, +5, +4, and -2 are independently non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, one or more or all internucleotidic linkages at positions +24, +23, +22, +19, +16, +15, +14, +13, +12, +11, +10, +6, +5, +4, -2, and -5 are independently non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, one or more or all internucleotidic linkages at positions +23, +22, +19, +16, +15, +14, +13, +12, +11, +10, +6, +5, +4, and -2 are independently non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, the first and last internucleotidic linkages of an oligonucleotide are

independently non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, the first and the last internucleotidic linkages and one or more or all internucleotidic linkages at positions +23, +22, +19, +16, +15, +14, +13, +12, +11, +10, +6, +5, +4, and -2 are independently non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, the first and the last internucleotidic linkages are both *R*p. In some embodiments, each phosphorothioate internucleotidic linkages are *S*p. In some embodiments, an internucleotidic linkage at position -2 is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -5 is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +5 is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +9 is a non-negatively charged internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +11 is a non-negatively charged internucleotidic linkage. In some embodiments, each of the internucleotidic linkages at positions -2, and -5 is independently a non-negatively charged internucleotidic linkage. In some embodiments, each of the internucleotidic linkages at positions +5, -2, and -5 is independently a non-negatively charged internucleotidic linkage. In some embodiments, each of the internucleotidic linkages at positions +11, +9, -2, and -5 is independently a non-negatively charged internucleotidic linkage. In some embodiments, each of the internucleotidic linkages at positions +11, +9, +5, -2, and -5 is independently a non-negatively charged internucleotidic linkage. In some embodiments, one or more or each of the 1st, 14th, 16th, 20th, 26th, and 29th internucleotidic linkages (unless otherwise specified, from the 5'-end) is independently a non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises no non-negatively charged internucleotidic linkages to the 5' side of a nucleoside opposite to a target adenosine except that the first internucleotidic linkage of an oligonucleotide may be optionally a non-negatively charged internucleotidic linkage. In some embodiments, an oligonucleotide comprises no internal non-negatively charged internucleotidic linkages except at position -2. In some embodiments, one or both of the first and last internucleotidic linkages of a first domain is independently a non-negatively charged internucleotidic linkage. In some embodiments, one or both of the first and last internucleotidic linkages of a second domain is independently a non-negatively charged internucleotidic linkage. In some embodiments, one or both of the first and last internucleotidic linkages of an oligonucleotide is independently a non-negatively charged internucleotidic linkage. In some embodiments, both of the first and last internucleotidic linkages of a first domain are independently non-negatively charged internucleotidic linkages. In some embodiments, both of the first and last internucleotidic linkages of a second domain are independently non-negatively charged internucleotidic linkages. In some embodiments, both of the first and last internucleotidic linkages of an oligonucleotide are independently non-negatively charged internucleotidic linkages. In some embodiments, each non-negatively charged internucleotidic linkage is independently a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, each non-negatively charged internucleotidic linkage is

independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, each non-negatively charged internucleotidic linkage is independently *Rp*, *Sp*, or non-chirally controlled. In some embodiments, one or more non-negatively charged internucleotidic linkages are independently not chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently not chirally controlled. In some embodiments, one or more non-negatively charged internucleotidic linkages are independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is *Rp*. In some embodiments, each non-negatively charged internucleotidic linkage is *Sp*. In some embodiments, an internucleotidic linkage, e.g., n001, bonded to an inosine or deoxyinosine or 2'-modified inosine (e.g., 2'-OH replaced with a non-H moiety such as –F, –OMe, –MOE, etc.) at its 3' position is non-chirally controlled or is chirally controlled and *Sp*. In some embodiments, it is chirally controlled and *Sp*. In some embodiments, oligonucleotides and compositions thereof comprising chirally controlled *Sp* non-negatively charged internucleotidic linkages (e.g., phosphoryl guanidine internucleotidic linkages such as n001) bonded to 3'-positions of nucleosides comprising hypoxanthine provide various advantages over corresponding stereorandom or *Rp* internucleotidic linkages, e.g., the same or better properties and/or activities, improved manufacturing efficiency, and/or lowered manufacturing cost, etc. In some embodiments, it was observed that processes for constructing chirally controlled *Sp* non-negatively charged internucleotidic linkages (e.g., phosphoryl guanidine internucleotidic linkages such as n001) bonded to 3'-positions of nucleosides comprising hypoxanthine can be performed more readily (e.g., higher reagent concentrations, smaller solution volumes, shorter reaction times, etc.) and/or with lower cost (e.g., more easily accessible materials).. In some embodiments, oligonucleotides and compositions thereof comprising chirally controlled *Rp* phosphorothioate internucleotidic linkages bonded to 3'-positions of nucleosides comprising hypoxanthine provide various advantages over corresponding stereorandom or *Sp* internucleotidic linkages, e.g., the same or better properties and/or activities, improved manufacturing efficiency, and/or lowered manufacturing cost, etc. In some embodiments, processes for constructing chirally controlled *Rp* phosphorothioate internucleotidic linkages bonded to 3'-positions of nucleosides comprising hypoxanthine can be performed more readily (e.g., higher reagent concentrations, smaller solution volumes, shorter reaction times, etc.) and/or with lower cost (e.g., more easily accessible materials).

[00929] In some embodiments, oligonucleotides comprise one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more, PN linkages. For example, in some embodiments, an oligonucleotide comprises one and no more than one PN linkage. In some embodiments, an oligonucleotide comprises two and no more than two PN linkages. In some embodiments, an oligonucleotide comprises three and no more than three PN linkages. In some embodiments, an oligonucleotide comprises four and no more than four PN linkages. In some embodiments, an oligonucleotide comprises five and no more than five PN linkages. In some embodiments, an oligonucleotide comprises five or more PN linkages. In some embodiments, PN linkages at certain

positions, e.g., 1, 2, 3, 4 or 5 of positions 1 (the internucleotidic linkage bonded to the first and second nucleosides from the 5'-end is at position 1; numbering increases toward the 3'-end), 14, 16, 26 and 29, provide higher editing levels than others. In some embodiments, position 29 is the last internucleotidic linkage position. In some embodiments, PN linkages are at two positions 1, 14, 16, 26 and 29. In some embodiments, PN linkages are at three positions 1, 14, 16, 26 and 29. In some embodiments, PN linkages are at four positions 1, 14, 16, 26 and 29. In some embodiments, PN linkages are at five positions 1, 14, 16, 26 and 29. In some embodiments, PN linkages are at positions 1 and 26. In some embodiments, they are at positions 14 and 29. In some embodiments, they are at positions 14 and 29. In some embodiments, they are at positions 26 and 29. In some embodiments, they are at positions 1, 14 and 26. In some embodiments, they are at positions 1, 26 and 29. In some embodiments, they are at positions 14, 16 and 26. In some embodiments, they are at positions 14, 16 and 29. In some embodiments, they are at positions 14, 26 and 29. In some embodiments, they are at positions 16, 26 and 29. In some embodiments, they are at positions 1, 14, 16 and 29. In some embodiments, they are at positions 1, 14, 26 and 29. In some embodiments, they are at positions 1, 16, 26 and 29. In some embodiments, they are at positions 14, 16, 26 and 29. In some embodiments, they are at positions 1, 14, 16, 26 and 29. In some embodiments, each such PN internucleotidic linkages is independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, each is independently n001. In some embodiments, each is independently n006.

[00930] In some embodiments, an oligonucleotide comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more, etc.) natural phosphate linkages. In some embodiments, both nucleosides bonded to a natural phosphate linkage are independently a 2'-modified sugar. In some embodiments, both nucleosides bonded to a majority (e.g., at least 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95% or more) of natural phosphate linkages are independently a 2'-modified sugar. In some embodiments, both nucleosides bonded to each natural phosphate linkage are independently a 2'-modified sugar. In some embodiments, a 2'-modified sugar is a bicyclic sugar or 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-modified sugar is independently a bicyclic sugar or 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-modified sugar is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-modified sugar is independently a 2'-OMe modified sugar or a 2'-MOE modified sugar. In some embodiments, each 2'-modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-modified sugar is independently a 2'-MOE modified sugar. In some embodiments, a natural phosphate linkage is utilized with a non-negatively charged internucleotidic linkage (e.g., a phosphoryl guanidine internucleotidic linkage such as n001). In some embodiments, an oligonucleotide comprises alternating natural phosphate linkages and non-negatively charged internucleotidic linkages (e.g., a phosphoryl guanidine internucleotidic linkage such as n001) (e.g., see WV-43047).

[00931] In some embodiments, one or more internucleotidic linkages at positions -1 and -2 are independently *R*p phosphorothioate internucleotidic linkages. In some embodiments, one or more

internucleotidic linkages at positions -3, -2, -1, +1, +3, +4, +5, +7, +8, +9, +10, +11, +12, +13,+16, +17 and +18 are independently *R*p phosphorothioate internucleotidic linkages. In some embodiments, an internucleotidic linkage at position -3 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -2 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -1 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +1 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +3 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +4 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +5 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +7 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +8 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +9 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +10 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +11 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +12 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +13 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +16 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +17 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +18 is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an oligonucleotide contains one and only one *R*p phosphorothioate internucleotidic linkage. In some embodiments, it contains two and no more than two. In some embodiments, it contains three and no more than three. In some embodiments, it contains four and no more than four. In some embodiments, it contains five and no more than five.

[00932] In some embodiments, a non-negatively charged internucleotidic linkage bonded to 3'-carbon of dI is *S*p. In some embodiments, a non-negatively charged internucleotidic linkage bonded to 3'-carbon of dI is *S*p. In some embodiments, a phosphoryl guanidine internucleotidic linkage bonded to 3'-carbon of dI is *S*p. In some embodiments, a n001 internucleotidic linkage bonded to 3'-carbon of dI is *S*p. In some embodiments, each non-negatively charged internucleotidic linkage bonded to 3'-carbon of dI is independently *S*p. In some embodiments, each neutral internucleotidic linkage bonded to 3'-carbon of dI is independently *S*p. In some embodiments, each phosphoryl guanidine internucleotidic linkage bonded to 3'-carbon of dI is independently *S*p. In some embodiments, each n001 bonded to 3'-carbon of dI is independently *S*p.

[00933] In some embodiments, a controlled level of oligonucleotides in a composition are desired oligonucleotides. In some embodiments, of all oligonucleotides in a composition that share a common base sequence (e.g., a desired sequence for a purpose), or of all oligonucleotides in a composition, level of desired

oligonucleotides (which may exist in various forms (e.g., salt forms) and typically differ only at non-chirally controlled internucleotidic linkages (various forms of the same stereoisomer can be considered the same for this purpose)) is about 5%-100%, 10%-100%, 20%-100%, 30%-100%, 40%-100%, 50%-100%, 60%-100%, 70%-100%, 80-100%, 90-100%, 95-100%, 50%-90%, about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, or at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99%. In some embodiments, a level is at least about 50%. In some embodiments, a level is at least about 60%. In some embodiments, a level is at least about 70%. In some embodiments, a level is at least about 75%. In some embodiments, a level is at least about 80%. In some embodiments, a level is at least about 85%. In some embodiments, a level is at least about 90%. In some embodiments, a level is or is at least $(DS)^{nc}$, wherein DS is about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% and nc is the number of chiral linkage phosphorus as described in the present disclosure (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 5-50, 5-40, 5-30, 5-25, 5-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more). In some embodiments, a level is or is at least $(DS)^{nc}$, wherein DS is about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% and nc is the number of chirally controlled internucleotidic linkages as described in the present disclosure (e.g., 1-50, 1-40, 1-30, 1-25, 1-20, 5-50, 5-40, 5-30, 5-25, 5-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 or more). In some embodiments, a level is or is at least $(DS)^{nc}$, wherein DS is 95%-100%.

[00934] Various types of internucleotidic linkages may be utilized in combination of other structural elements, e.g., sugars, to achieve desired oligonucleotide properties and/or activities. For example, the present disclosure routinely utilizes modified internucleotidic linkages and modified sugars, optionally with natural phosphate linkages and natural sugars, in designing oligonucleotides. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars. In some embodiments, the present disclosure provides an oligonucleotide comprising one or more modified sugars and one or more modified internucleotidic linkages, one or more of which are natural phosphate linkages.

[00935] In some embodiments, provided oligonucleotides comprise a number of natural RNA sugars (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, two or more or all of them are optionally consecutive). In some embodiments, such oligonucleotides comprise modified sugars, e.g., 2' modified sugars (e.g., 2'-F, etc.) and/or 2'-OR modified sugars wherein R is not –H (e.g., 2-OMe, 2-MOE, etc.) at one or both ends, and/or various modified internucleotidic linkages (e.g., phosphorothioate internucleotidic linkages, non-negatively charged internucleotidic linkages, etc.). In some embodiments, at the 5'-end there are one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 more such 2'-OR modified sugars, wherein R is not –H. In some embodiments, at the 3'-end there are one or more, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 more such 2'-OR modified sugars, wherein R is not –H. In some embodiments, each 2'-modified sugar is independently a 2'-OR modified sugar wherein R is not –H. In some embodiments, as described herein, 2'-OR is 2'-OMe. In some embodiments, 2'-OR is 2'-MOE. In some embodiments, each of 2'-OR is

independently 2'-OMe or 2'-MOE. In some embodiments, each 2'-OR is 2'-OMe.

[00936] In some embodiments, stability of various internucleotidic linkages is assessed. In some embodiments, internucleotidic linkages are exposed to various conditions utilized for oligonucleotide manufacturing, e.g., solid phase oligonucleotide synthesis, including reagents, solvents, temperatures (in some cases, temperatures higher than room temperature), cleavage conditions, deprotection conditions, purification conditions, etc., and stability is assessed. In some embodiments, stable internucleotidic linkages (e.g., those having no more than than 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, 1%, 0.9%, 0.8%, 0.7%, 0.6%, 0.5%, 0.4%, 0.3%, 0.2%, or 0.1% degradation when exposed to one or more conditions and/or processes, or after a complete oligonucleotide manufacturing process) are selected for utilization in various oligonucleotide compositions and applications.

[00937] In some embodiments, an internucleotidic linkage between N_{23} and N_{22} is a natural phosphate linkage. In some embodiments, an internucleotidic linkage between N_{22} and N_{21} is a natural phosphate linkage. In some embodiments, an internucleotidic linkage between N_{17} and N_{16} is a natural phosphate linkage. In some embodiments, an internucleotidic linkage between N_{11} and N_{10} is a natural phosphate linkage. In some embodiments, an internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage. In some embodiments, an internucleotidic linkage between N_2 and N_3 is a natural phosphate linkage.

[00938] In some embodiments, an internucleotidic linkage between N_8 and N_7 is a phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_8 and N_7 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a 17th internucleotidic linkage from the 5'-end of an oligonucleotide is a phosphorothioate internucleotidic linkage. In some embodiments, a 17th internucleotidic linkage from the 5'-end of an oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_6 and N_5 is a phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_6 and N_5 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a 19th internucleotidic linkage from the 5'-end of an oligonucleotide is a phosphorothioate internucleotidic linkage. In some embodiments, a 19th internucleotidic linkage from the 5'-end of an oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_{13} and N_{12} is a phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_{13} and N_{12} is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a 12th internucleotidic linkage from the 5'-end of an oligonucleotide is a phosphorothioate internucleotidic linkage. In some embodiments, a 12th internucleotidic linkage from the 5'-end of an oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_9 and N_8 is a phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage between N_9 and N_8 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, a 16th internucleotidic linkage from the 5'-end of an oligonucleotide is a phosphorothioate internucleotidic linkage. In some embodiments, a 16th internucleotidic linkage from the 5'-end of an oligonucleotide is a *Sp* phosphorothioate internucleotidic

linkage.

[00939] In some embodiments, an internucleotidic linkage between N_{24} and N_{23} is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an internucleotidic linkage between N_{13} and N_{12} is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an internucleotidic linkage between N_{12} and N_{11} is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an internucleotidic linkage between N_{13} and N_{12} is a PN linkage and an internucleotidic linkage between N_{12} and N_{11} is a PN linkage. In some embodiments, each linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, each linkage is n001. In some embodiments, it is n006. In some embodiments, each linkage is methylphosphonate. In some embodiments, each linkage MsPA. In some embodiments, one linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, one linkage is n001. In some embodiments, it is n006. In some embodiments, one linkage is methylphosphonate. In some embodiments, one linkage MsPA. In some embodiments, an internucleotidic linkage between N_9 and N_8 is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an internucleotidic linkage between N_{-1} and N_{-2} is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, an internucleotidic linkage between N_{-4} and N_{-5} is a PN linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA. In some embodiments, a first internucleotidic linkage from the 5'-end of the oligonucleotide is a PN internucleotidic linkage. In some embodiments, it is a phosphoryl guanidine internucleotidic linkage. In some embodiments, it is n001. In some embodiments, it is n006. In some embodiments, it is methylphosphonate. In some embodiments, it is MsPA.

Additional Chemical Moieties

[00940] In some embodiments, an oligonucleotide comprises one or more additional chemical moieties. Various additional chemical moieties, e.g., targeting moieties, carbohydrate moieties, lipid moieties, etc. are known in the art and can be utilized in accordance with the present disclosure to modulate properties and/or activities of provided oligonucleotides, e.g., stability, half life, activities, delivery, pharmacodynamics properties, pharmacokinetic properties, etc. In some embodiments, certain additional chemical moieties facilitate delivery of oligonucleotides to desired cells, tissues and/or organs, including but not limited the cells

of the central nervous system. In some embodiments, certain additional chemical moieties facilitate internalization of oligonucleotides. In some embodiments, certain additional chemical moieties increase oligonucleotide stability. In some embodiments, the present disclosure provides technologies for incorporating various additional chemical moieties into oligonucleotides.

[00941] In some embodiments, an additional chemical moiety is or comprises a small molecule moiety. In some embodiments, a small molecule is a ligand of a protein (e.g., receptor). In some embodiments, a small molecule binds to a polypeptide. In some embodiments, a small molecule is an inhibitor of a polypeptide. In some embodiments, an additional chemical moiety is or comprises a peptide moiety (e.g., an antibody). In some embodiments, an additional chemical moiety is or comprises a nucleic acid moiety. In some embodiments, a nucleic acid provides a new property and/or activity. In some embodiments, a nucleic acid moiety forms a duplex or other secondary structure with the original oligonucleotide chain (before conjugation) or a portion thereof. In some embodiments, a nucleic acid is or comprises an oligonucleotide targeting the same or a different target, and may perform its activity through the same or a different mechanism. In some embodiments, a nucleic acid is or comprises a RNAi agent. In some embodiments, a nucleic acid is or comprises a miRNA agent. In some embodiments, a nucleic acid is or comprises RNase H dependent. In some embodiments, a nucleic acid is or comprises a gRNA. In some embodiments, a nucleic acid is or comprises an aptamer. In some embodiments, an additional chemical moiety is or comprises a carbohydrate moiety as described herein. Many useful agents, e.g., small molecules, peptides, carbohydrates, nucleic acid agents, etc., may be conjugated with oligonucleotides herein in accordance with the present disclosure.

[00942] In some embodiments, an oligonucleotide comprises an additional chemical moiety demonstrates increased delivery to and/or activity in an tissue compared to a reference oligonucleotide, e.g., a reference oligonucleotide which does not have the additional chemical moiety but is otherwise identical.

[00943] In some embodiments, non-limiting examples of additional chemical moieties include carbohydrate moieties, targeting moieties, etc., which, when incorporated into oligonucleotides, can improve one or more properties. In some embodiments, an additional chemical moiety is selected from: glucose, GluNAc (N-acetyl amine glucosamine) and anisamide moieties. In some embodiments, a provided oligonucleotide can comprise two or more additional chemical moieties, wherein the additional chemical moieties are identical or non-identical, or are of the same category (e.g., carbohydrate moiety, sugar moiety, targeting moiety, etc.) or not of the same category.

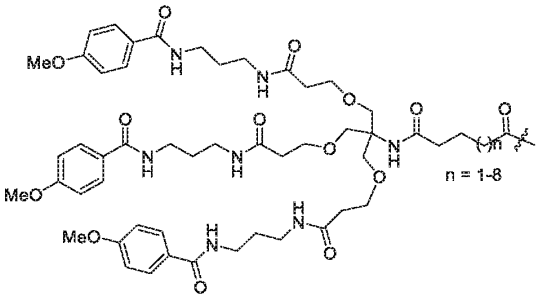
[00944] In some embodiments, an additional chemical moiety is a targeting moiety. In some embodiments, an additional chemical moiety is or comprises a carbohydrate moiety. In some embodiments, an additional chemical moiety is or comprises a lipid moiety. In some embodiments, an additional chemical moiety is or comprises a ligand moiety for, e.g., cell receptors such as a sigma receptor, an asialoglycoprotein receptor, etc. In some embodiments, a ligand moiety is or comprises an anisamide moiety, which may be a ligand moiety for a sigma receptor. In some embodiments, a ligand moiety is or comprises a GalNAc moiety, which may be a ligand moiety for an asialoglycoprotein receptor. In some embodiments, an additional chemical moiety

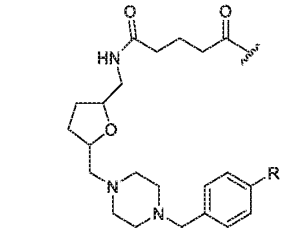
facilitates delivery to liver.

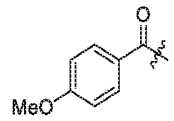
[00945] In some embodiments, a provided oligonucleotide can comprise one or more linkers and additional chemical moieties (e.g., targeting moieties), and/or can be chirally controlled or not chirally controlled, and/or have a bases sequence and/or one or more modifications and/or formats as described herein.

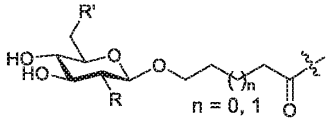
[00946] Various linkers, carbohydrate moieties and targeting moieties, including many known in the art, can be utilized in accordance with the present disclosure. In some embodiments, a carbohydrate moiety is a targeting moiety. In some embodiments, a targeting moiety is a carbohydrate moiety.

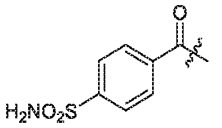
[00947] In some embodiments, a provided oligonucleotide comprises an additional chemical moiety suitable for delivery, e.g., glucose, GluNAc (N-acetyl amine glucosamine), anisamide, or a structure selected from:

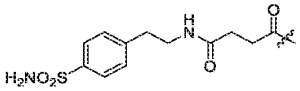




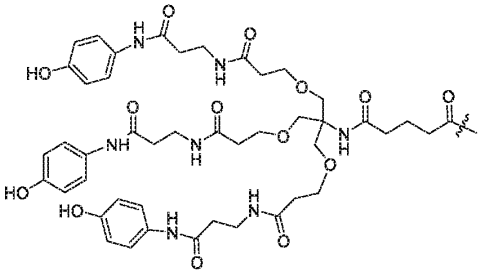


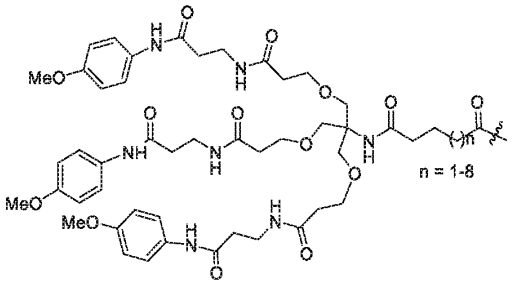


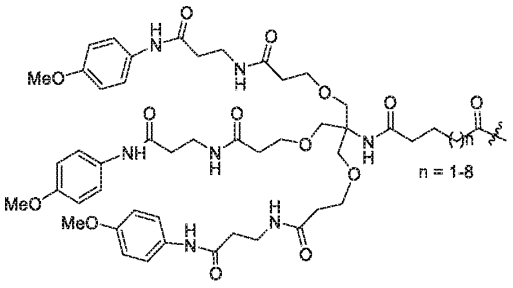




R = NHAc, R' = OH; R = NHCOC6H4OMe(p-anisoyl), R'=OH;
R = NHAc, R' = NHCOC6H4OMe(p-anisoyl);
R = OH, R' = NHCOC6H4OMe(p-anisoyl)







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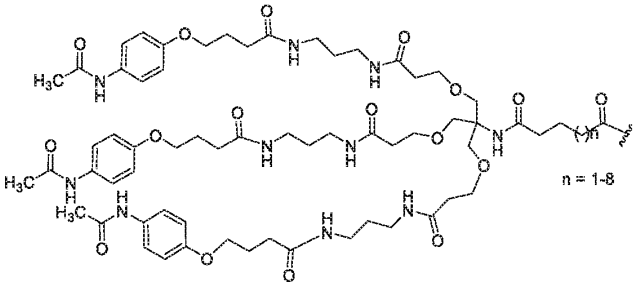


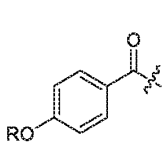
. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, n is 6. In some embodiments, n is 7. In some embodiments, n is 8.

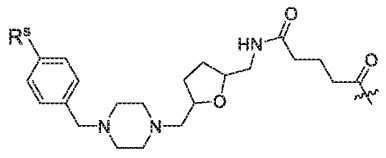
[00948] In some embodiments, additional chemical moieties are any of ones described in the Examples, including examples of various additional chemical moieties incorporated into various oligonucleotides.

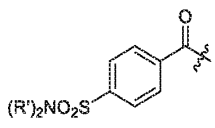
[00949] In some embodiments, an additional chemical moiety conjugated to an oligonucleotide is capable of targeting the oligonucleotide to a cell in the central nervous system.

[00950] In some embodiments, an additional chemical moiety comprises or is a cell receptor ligand. In some embodiments, an additional chemical moiety comprises or is a protein binder, e.g., one binds to a cell surface protein. Such moieties among other things can be useful for targeted delivery of oligonucleotides to cells expressing the corresponding receptors or proteins. In some embodiments, an additional chemical moiety of a provided oligonucleotide comprises anisamide or a derivative or an analog thereof and is capable of targeting the oligonucleotide to a cell expressing a particular receptor, such as the sigma 1 receptor.

[00951] In some embodiments, a provided oligonucleotide is formulated for administration to a body cell and/or tissue expressing its target. In some embodiments, an additional chemical moiety conjugated to an oligonucleotide is capable of targeting the oligonucleotide to a cell.

[00952] In some embodiments, an additional chemical moiety is selected from optionally substituted phenyl, 

, 

, 

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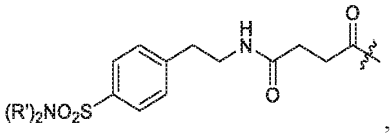
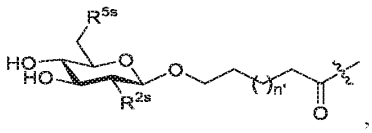
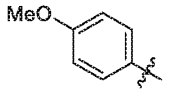
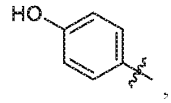
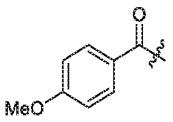
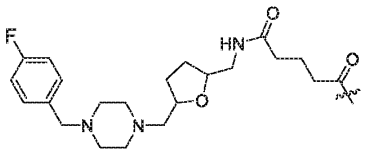
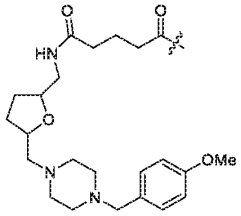
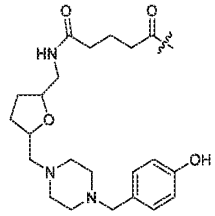
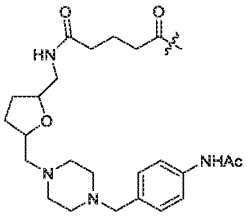
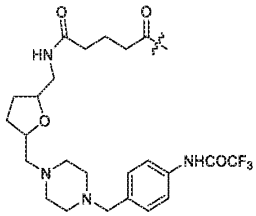
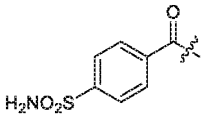
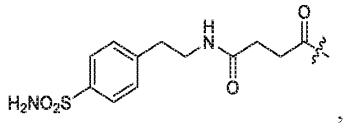
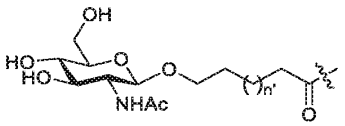
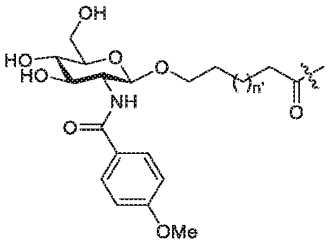
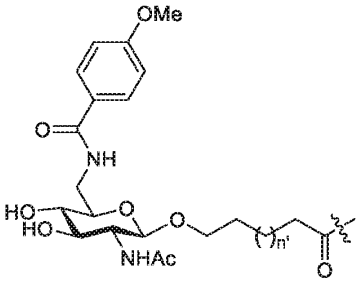
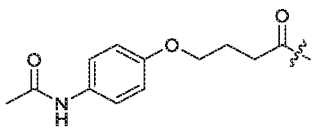
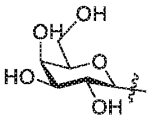
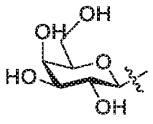
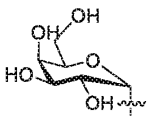
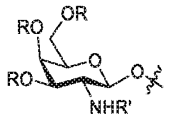
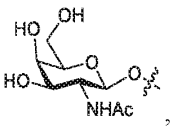
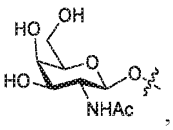
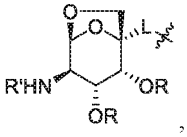
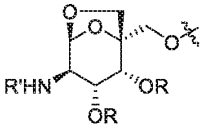
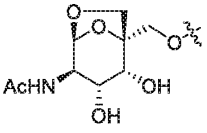


, and , wherein n' is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, and each other variable is as described in the present disclosure. In some embodiments, R^s is F. In some embodiments, R^s is OMe. In some embodiments, R^s is OH. In some embodiments, R^s is NHAc. In some embodiments, R^s is $NHCOCF_3$. In some embodiments, R' is H. In some embodiments, R is H. In some embodiments, R^{2s} is NHAc, and R^{5s} is OH. In some embodiments, R^{2s} is p-anisoyl, and R^{5s} is OH. In some embodiments, R^{2s} is NHAc and R^{5s} is p-anisoyl. In some embodiments, R^{2s} is OH, and R^{5s} is p-anisoyl. In some embodiments, an additional chemical moiety is selected from

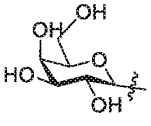













, and . In some embodiments, n' is 1. In

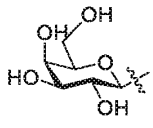
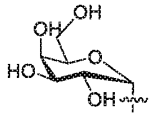
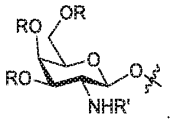
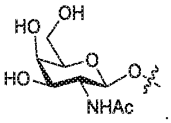
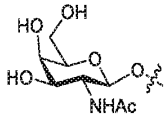
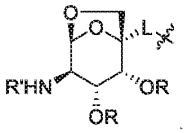
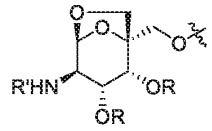
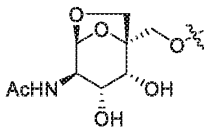
some embodiments, n' is 0. In some embodiments, n" is 1. In some embodiments, n" is 2.

[00953] In some embodiments, an additional chemical moiety is or comprises an asialoglycoprotein receptor (ASGPR) ligand.

[00954] Without wishing to be bound by any particular theory, the present disclosure notes that ASGPR1 has also been reported to be expressed in the hippocampus region and/or cerebellum Purkinje cell layer of the mouse. http://mouse.brain-map.org/experiment/show/2048

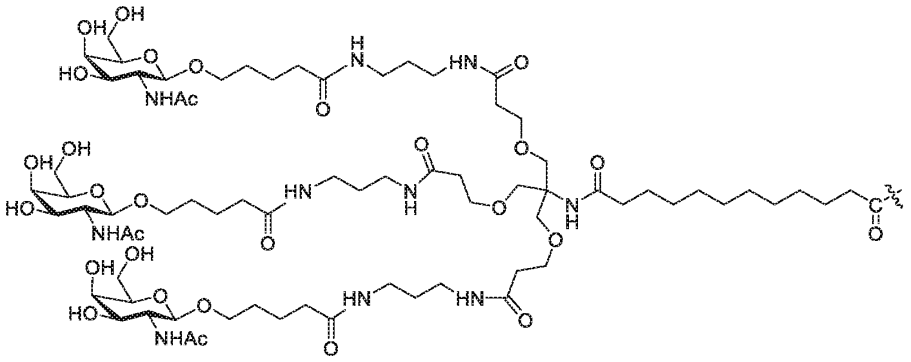
[00955] Various other ASGPR ligands are known in the art and can be utilized in accordance with the present disclosure. In some embodiments, an ASGPR ligand is a carbohydrate. In some embodiments, an ASGPR ligand is GalNac or a derivative or an analog thereof. In some embodiments, an ASGPR ligand is one described in Sanhueza et al. J. Am. Chem. Soc., 2017, 139 (9), pp 3528–3536. In some embodiments, an ASGPR ligand is one described in Mamidyala et al. J. Am. Chem. Soc., 2012, 134, pp 1978−1981. In some embodiments, an ASGPR ligand is one described in US 20160207953. In some embodiments, an ASGPR ligand is a substituted-6,8-dioxabicyclo[3.2.1]octane-2,3-diol derivative disclosed in, e.g., US 20160207953. In some embodiments, an ASGPR ligand is one described in, e.g., US 20150329555. In some embodiments, an ASGPR ligand is a substituted-6,8-dioxabicyclo[3.2.1]octane-2,3-diol derivative disclosed e.g., in US 20150329555. In some embodiments, an ASGPR ligand is one described in US 8877917, US 20160376585, US 10086081, or US 8106022. In some embodiments, various GalNAc derivatives and uses thereof are described in WO 2022/076922 and can be utilized in accordance with the present disclosure. ASGPR ligands described in these documents are incorporated herein by reference. Those skilled in the art will appreciate that various technologies are known in the art, including those described in these documents, for assessing binding of a chemical moiety to ASGPR and can be utilized in accordance with the present disclosure. In some embodiments, a provided oligonucleotide is conjugated to an ASGPR ligand. In some embodiments, a provided oligonucleotide comprises an ASGPR ligand. In some embodiments, an additional chemical moiety comprises an ASGPR ligand is , , , , , , , , or , wherein each variable is independently as described in the present disclosure. In some embodiments, R is −H. In some embodiments, R' is −C(O)R.

[00956] In some embodiments, an additional chemical moiety is or comprises . In some

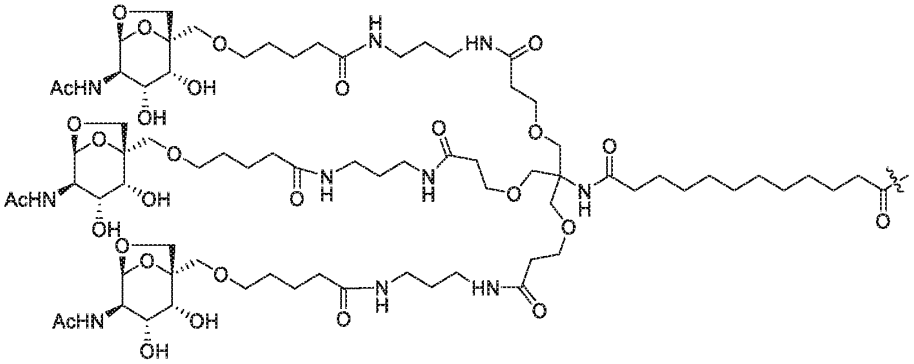
embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises optionally substituted . In some embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises . In some embodiments, an additional chemical moiety is or comprises .

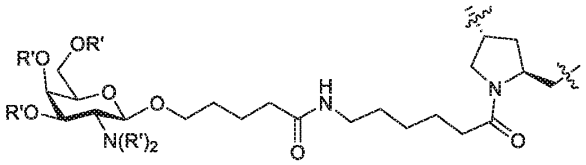
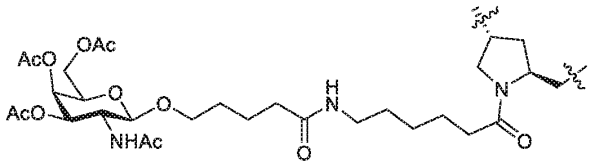
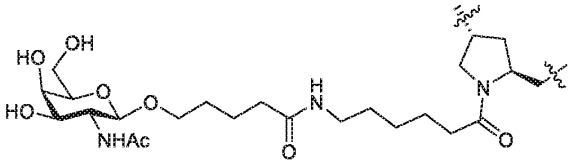
[00957] In some embodiments, an additional chemical moiety comprises one or more moieties that can bind to, e.g., oligonucleotide target cells. For example, in some embodiments, an additional chemistry moiety comprises one or more protein ligand moieties, e.g., in some embodiments, an additional chemical moiety comprises multiple moieties, each of which independently is an ASGPR ligand. In some embodiments, as in Mod 001 and Mod083, an additional chemical moiety comprises three such ligands.

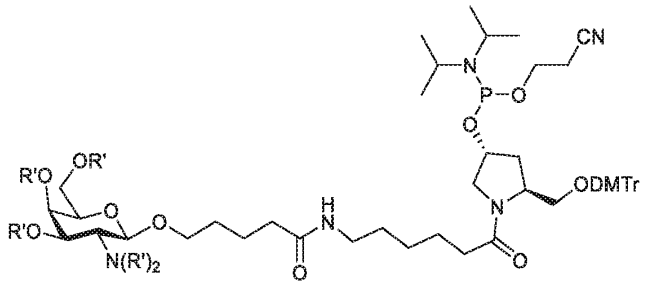
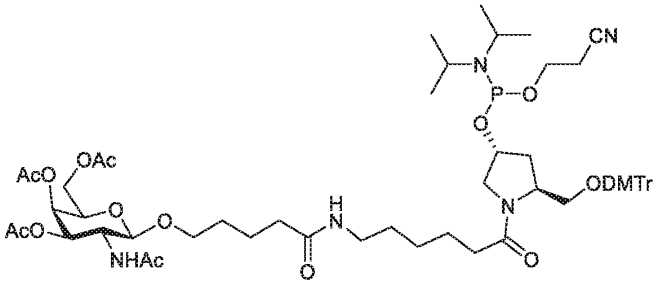
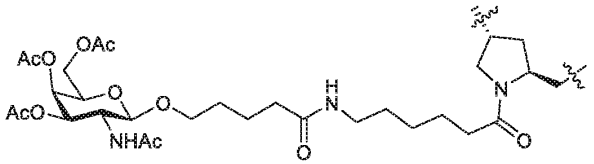
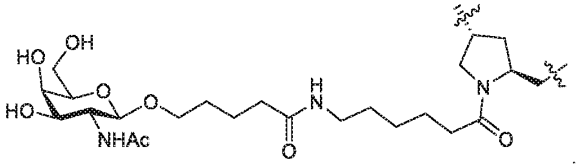
Mod001:

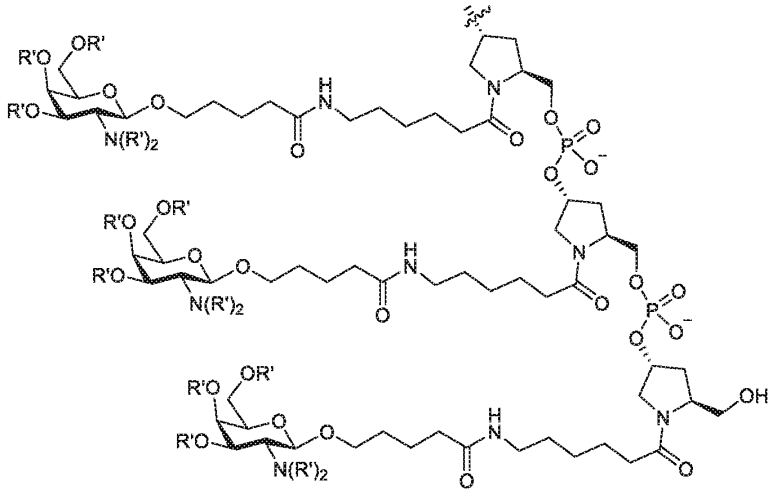


Mod083:

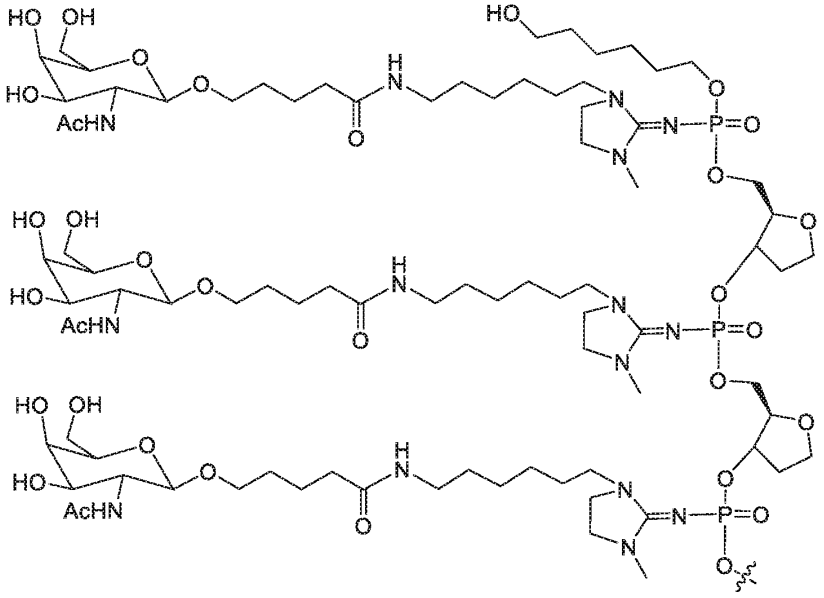


[00958] In some embodiments, an oligonucleotide comprises , wherein each variable is independently as described herein. In some embodiments, each –OR' is –OAc, and –N(R')$_2$ is –NHAc. In some embodiments, an oligonucleotide comprises . In some embodiments, each R' is –H. In some embodiments, each –OR' is –OH, and each –N(R')$_2$ is –NHC(O)R. In some embodiments, each –OR' is –OH, and each –N(R')$_2$ is –NHAc. In some embodiments, an oligonucleotide comprises  (L025). In some

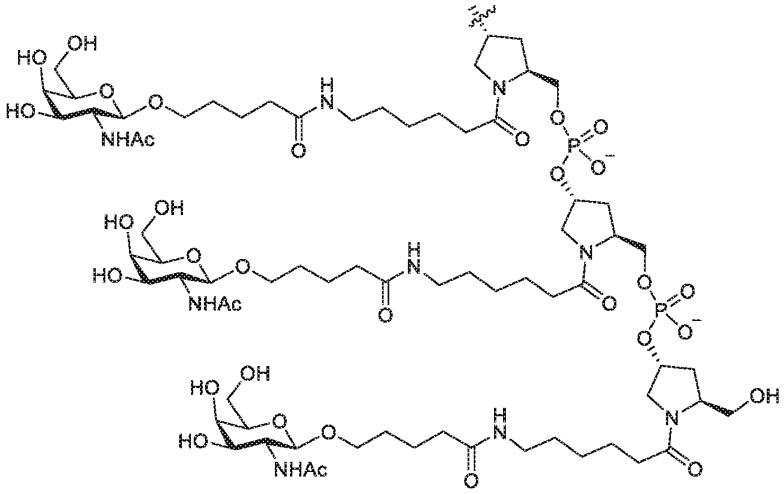
embodiments, the $-CH_2-$ connection site is utilized as a C5 connection site in a sugar. In some embodiments, the connection site on the ring is utilized as a C3 connection site in a sugar. Such moieties may be introduced utilizing, e.g., phosphoramidites such as , e.g.,  (those skilled in the art appreciate that one or more other groups, such as protection groups for $-OH$, $-NH_2-$, $-N(i\text{-}Pr)_2$, $-OCH_2CH_2CN$, etc., may be alternatively utilized, and protection groups can be removed under various suitable conditions, sometimes during oligonucleotide de-protection and/or cleavage steps). In some embodiments, an oligonucleotide comprises 2, 3 or more (e.g., 3 and no more than 3) . In some embodiments, an oligonucleotide comprises 2, 3 or more (e.g., 3 and no more than 3) . In some embodiments, copies of such moieties are linked by internucleotidic linkages, e.g., natural phosphate linkages, as described herein. In some embodiments, when at a 5'-end, a $-CH_2-$ connection site is bonded to $-OH$. In some embodiments, an



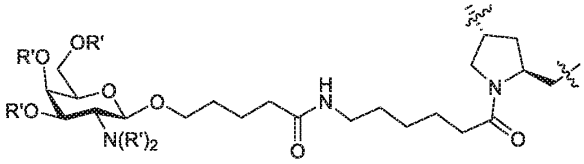
oligonucleotide comprises . In some embodiments, an oligonucleotide comprises

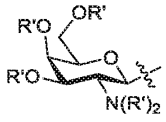
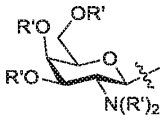


. In some embodiments, each −OR` is −OAc, and −N(R`)$_2$ is −NHAc. In some embodiments, an oligonucleotide comprises



. Among other things,



may be utilized to introduce  with comparable and/or better activities and/or properties. In some embodiments, it provides improved preparation efficiency and/or lower cost for the same number of  (e.g., when compared to Mod001).

[00959] In some embodiments, an additional chemical moiety is described herein, e.g., in Table 1 or Table 1A.

[00960] In some embodiments, an additional chemical moiety is Mod001. In some embodiments, an additional chemical moiety is Mod083. In some embodiments, an additional chemical moiety, e.g., a Mod group, is directly conjugated (e.g., without a linker) to the remainder of the oligonucleotide. In some embodiments, an additional chemical moiety is conjugated via a linker to the remainder of the oligonucleotide. In some embodiments, additional chemical moieties, e.g., Mod groups, may be directly connected, and/or via a linker, to nucleobases, sugars and/or internucleotidic linkages of oligonucleotides. In some embodiments, Mod groups are connected, either directly or via a linker, to sugars. In some embodiments, Mod groups are connected, either directly or via a linker, to 5'-end sugars. In some embodiments, Mod groups are connected, either directly or via a linker, to 5'-end sugars via 5' carbon. For examples, see various oligonucleotides in Table 1 and Table 1A. In some embodiments, Mod groups are connected, either directly or via a linker, to 3'-end sugars. In some embodiments, Mod groups are connected, either directly or via a linker, to 3'-end sugars via 3' carbon. In some embodiments, Mod groups are connected, either directly or via a linker, to nucleobases. In some embodiments, Mod groups are connected, either directly or via a linker, to internucleotidic linkages.

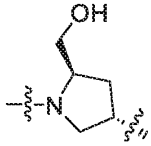
In some embodiments, provided oligonucleotides comprise Mod001 connected to 5'-end of oligonucleotide chains through L001.

[00961] As appreciated by those skilled in the art, an additional chemical moiety may be connected to an oligonucleotide chain at various locations, e.g., 5'-end, 3'-end, or a location in the middle (e.g., on a sugar, a base, an internucleotidic linkage, etc.). In some embodiments, it is connected at a 5'-end. In some embodiments, it is connected at a 3'-end. In some embodiments, it is connected at a nucleotide in the middle.

[00962] Certain additional chemical moieties (e.g., lipid moieties, targeting moieties, carbohydrate moieties), including but not limited to Mod012, Mod039, Mod062, Mod085, Mod086, and Mod094, and various linkers for connecting additional chemical moieties to oligonucleotide chains, including but not limited to L001, L003, L004, L008, L009, and L010, are described in WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the additional chemical moieties and linkers of each of which are independently incorporated herein by reference, and can be utilized in accordance with the present disclosure. In some embodiments, an additional chemical moiety is digoxigenin or biotin or a derivative thereof.

[00963] In some embodiments, an oligonucleotide comprises a linker, e.g., L001 L004, L008, and/or an additional chemical moiety, e.g., Mod012, Mod039, Mod062, Mod085, Mod086, or Mod094. In some embodiments, a linker, *e.g.*, L001, L003, L004, L008, L009, L110, *etc.* is linked to a Mod, *e.g.*, Mod012, Mod039, Mod062, Mod085, Mod086, Mod094, *etc.*

L001: $-NH-(CH_2)_6-$ linker (also known as a C6 linker, C6 amine linker or C6 amino linker), connected to Mod, if any, through −NH−, and the 5'-end or 3'-end of the oligonucleotide chain through either a phosphate linkage (−O−P(O)(OH)−O−, which may exist as a salt form, and may be indicated as O or PO) or a phosphorothioate linkage (−O−P(O)(SH)−O−, which may exist as a salt form, and may be indicated as * if the phosphorothioate is not chirally controlled; or *S, S, or *Sp*, if the phosphorothioate is chirally controlled and has an *Sp* configuration, or *R, R, or *Rp*, if the phosphorothioate is chirally controlled and has an *Rp* configuration) as indicated at the $-CH_2-$ connecting site. If no Mod is present, L001 is connected to −H through −NH−;

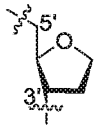
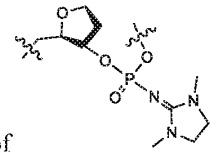
L003:  linker. In some embodiments, it is connected to Mod, if any (if no Mod, −H), through its amino group, and the 5'-end or 3'-end of an oligonucleotide chain e.g., via a linkage (e.g., a phosphate linkage (O or PO) or a phosphorothioate linkage (can be either not chirally controlled or chirally controlled (*Sp* or *Rp*)));

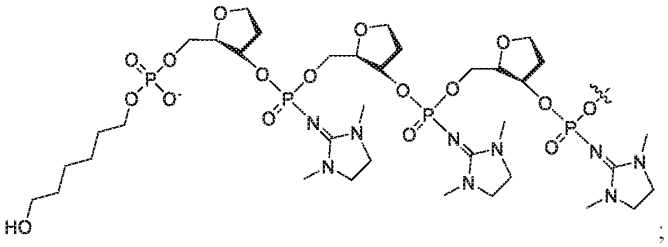
L004: linker having the structure of $-NH(CH_2)_4CH(CH_2OH)CH_2-$, wherein −NH− is connected to Mod

(through –C(O)–) or –H, and the –CH_2– connecting site is connected to an oligonucleotide chain (e.g., at the 3'-end) through a linkage, e.g., phosphodiester (–O–P(O)(OH)–O–, which may exist as a salt form, and may be indicated as O or PO), phosphorothioate (–O–P(O)(SH)–O–, which may exist as a salt form, and may be indicated as * if the phosphorothioate is not chirally controlled; or *S, S, or *Sp*, if the phosphorothioate is chirally controlled and has an *Sp* configuration, or *R, R, or *Rp*, if the phosphorothioate is chirally controlled and has an *Rp* configuration), or phosphorodithioate (–O–P(S)(SH)–O–, which may exist as a salt form, and may be indicated as PS2 or : or D) linkage. For example, an asterisk immediately preceding a L004 (e.g., *L004) indicates that the linkage is a phosphorothioate linkage, and the absence of an asterisk immediately preceding L004 indicates that the linkage is a phosphodiester linkage. For example, in an oligonucleotide which terminates in ...mAL004, the linker L004 is connected (via the –CH_2– site) through a phosphodiester linkage to the 3' position of the 3'-terminal sugar (which is 2'-OMe modified and connected to the nucleobase A), and the L004 linker is connected via –NH– to –H. Similarly, in one or more oligonucleotides, the L004 linker is connected (via the –CH_2– site) through the phosphodiester linkage to the 3' position of the 3'-terminal sugar, and the L004 is connected via –NH– to, e.g., Mod012, Mod085, Mod086, etc.;

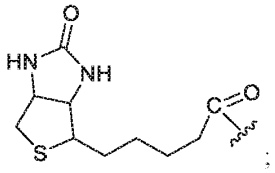
L008: linker having the structure of –C(O)–$(CH_2)_9$–, wherein –C(O)– is connected to Mod (through –NH–) or –OH (if no Mod indicated), and the –CH_2– connecting site is connected to an oligonucleotide chain (e.g., at the 5'-end) through a linkage, e.g., phosphodiester (–O–P(O)(OH)–O–, which may exist as a salt form, and may be indicated as O or PO), phosphorothioate (–O–P(O)(SH)–O–, which may exist as a salt form, and may be indicated as * if the phosphorothioate is not chirally controlled; or *S, S, or *Sp*, if the phosphorothioate is chirally controlled and has an *Sp* configuration, or *R, R, or *Rp*, if the phosphorothioate is chirally controlled and has an *Rp* configuration), or phosphorodithioate (–O–P(S)(SH)–O–, which may exist as a salt form, and may be indicated as PS2 or : or D) linkage. For example, in an example oligonucleotide which has the sequence of 5'-L008mN * mN * mN * mN * N * N * N * N * N * N * N * N * N * mN * mN * mN * mN-3', and which has a Stereochemistry/Linkage of OXXXXXXXXX XXXXXXXX, wherein N is a base, wherein O is a natural phosphate internucleotidic linkage, and wherein X is a stereorandom phosphorothioate, L008 is connected to –OH through –C(O)–, and the 5'-end of an oligonucleotide chain through a phosphate linkage (indicated as "O" in "Stereochemistry/Linkage"); in another example oligonucleotide, which has the sequence of 5'-Mod062L008mN * mN * mN * mN * N * N * N * N * N * N * N * N * N * N * mN * mN * mN * mN-3', and which has a Stereochemistry/Linkage of OXXXXXXXXX XXXXXXXX, wherein N is a base, L008 is connected to Mod062 through –C(O)–, and the 5'-end of an oligonucleotide chain through a phosphate linkage (indicated as "O" in "Stereochemistry/Linkage");

L009: –$CH_2CH_2CH_2$–. In some embodiments, when L009 is present at the 5'-end of an oligonucleotide without a Mod, one end of L009 is connected to –OH and the other end connected to a 5'-carbon of the oligonucleotide chain e.g., via a linkage (e.g., a phosphate linkage (O or PO) or a phosphorothioate linkage (can be either not chirally controlled or chirally controlled (*Sp* or *Rp*)));

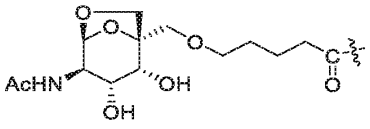
L010: . L010 connects to other moieties, e.g., L023, L010, oligonucleotide chains, etc., through various linkages (e.g., n001; if not indicated, typically phosphates). When no other moieties are present, L010 is bonded to –OH. For example in various oligonucleotides, L010 is utilized with n001R to form L010n001R, which has the structure of  and wherein the configuration of linkage phosphorus is *R*p. In some embodiments, multiple L010n001R may be utilized. For example, various oligonucleotides comprise L023L010n001RL010n001RL010n001R, which has the following structure (which is bonded to the 5'-carbon at the 5'-end of the oligonucleotide chain, and each linkage phosphorus is independently *R*p):

;

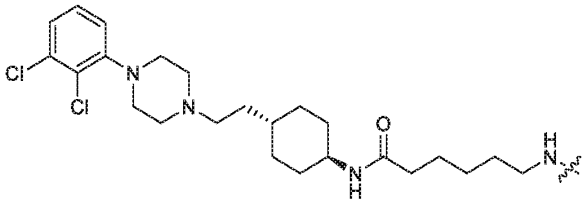
Mod012 (in some embodiments, –C(O)– connects to –NH– of a linker such as L001, L004, L008, *etc.*):

;

Mod039 (in some embodiments, –C(O)– connects to –NH– of a linker such as L001, L003, L004, L008, L009, L110, *etc.*):

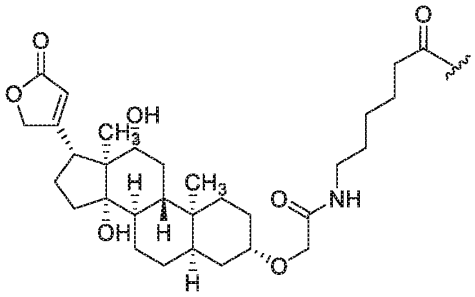


Mod062 (in some embodiments, –C(O)– connects to –NH– of a linker such as L001, L003, L004, L008, L009, L110, *etc.*):



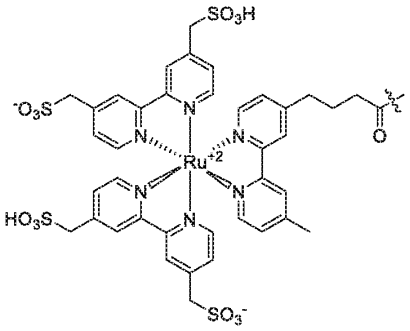
;

Mod085 (in some embodiments, –C(O)– connects to –NH– of a linker such as L001, L003, L004, L008, L009, L110, *etc.*):



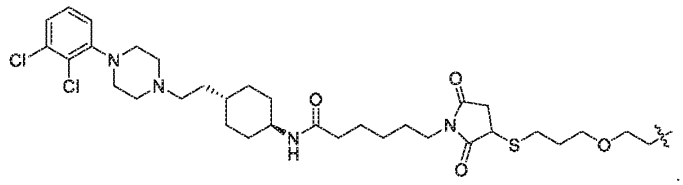
;

Mod086 (in some embodiments, –C(O)– connects to –NH– of a linker such as L001, L003, L004, L008, L009, L110, *etc.*):



;

Mod094 (in some embodiments, connects to an internucleotidic linkage, or to the 5'-end or 3'-end of an oligonucleotide via a linkage, *e.g.*, a phosphate linkage, a phosphorothioate linkage (which is optionally chirally controlled), *etc.*. For example, in an example oligonucleotide which has the sequence of 5'-mN * mN * mN * mN * N * N * N * N * N * N * N * N * N * N * mN * mN * mN * mNMod094-3', and which has a Stereochemistry/Linkage of XXXXX XXXXX XXXXX XXO, wherein N is a base, Mod094 is connected to the 3'-end of the oligonucleotide chain (3'-carbon of the 3'-end sugar) through a phosphate group (which is not shown below and which may exist as a salt form; and which is indicated as "O" in "Stereochemistry/Linkage" (...XXXX**O**))):



[00964] In some embodiments, an additional chemical moiety (e.g., a linker, lipid, solubilizing group, conjugate group, targeting group, and/or targeting ligand) is one described in WO 2012/030683 or WO 2021/030778. In some embodiments, a provided oligonucleotide comprise a chemical structure (e.g. , a linker, lipid, solubilizing group, and/or targeting ligand) described in WO 2012/030683, WO 2021/030778, WO 2019112485, US 20170362270, WO 2018156056, or WO 2018056871, WO 2021/030778, WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, or WO 2020/252376.

[00965] In some embodiments, a provide oligonucleotide comprises an additional chemical moiety (e.g., a targeting group, a conjugate group, etc.) and/or a modification (e.g., of nucleobase, sugar, internucleotidic linkage, etc.) described in: U.S. Pat. Nos. 5,688,941; 6,294,664; 6,320,017; 6,576,752; 5,258,506; 5,591,584; 4,958,013; 5,082,830; 5,118,802; 5,138,045; 6,783,931; 5,254,469; 5,414,077; 5,486,603; 5,112,963; 5,599,928; 6,900,297; 5,214,136; 5,109,124; 5,512,439; 4,667,025; 5,525,465; 5,514,785; 5,565,552; 5,541,313; 5,545,730; 4,835,263; 4,876,335; 5,578,717; 5,580,731; 5,451,463; 5,510,475; 4,904,582; 5,082,830; 4,762,779; 4,789,737; 4,824,941; 4,828,979; 5,595,726; 5,214,136; 5,245,022; 5,317,098; 5,371,241; 5,391,723; 4,948,882; 5,218,105; 5,112,963; 5,567,810; 5,574,142; 5,578,718; 5,608,046; 4,587,044; 4,605,735; 5,585,481; 5,292,873; 5,552,538; 5,512,667; 5,597,696; 5,599,923; 7,037,646; 5,587,371; 5,416,203; 5,262,536; 5,272,250; or 8,106,022.

[00966] In some embodiments, an additional chemical moiety, e.g., a Mod, is connected via a linker. Various linkers are available in the art and may be utilized in accordance with the present disclosure, for example, those utilized for conjugation of various moieties with proteins (e.g., with antibodies to form antibody-drug conjugates), nucleic acids, etc. Certain useful linkers are described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the linker moieties of each of which are independently incorporated herein by reference. In some embodiments, a linker is, as non-limiting examples, L001, L004, L009 or L010. In some embodiments, an oligonucleotide comprises a linker, but not an additional chemical moiety other than the linker. In some embodiments, an oligonucleotide comprises a linker, but not an additional chemical moiety other than the linker, wherein the linker is L001, L004, L009, or L010. In some embodiments, a linker is or comprises a moiety having the structure of an internucleotidic linkage as described herein. In some embodiments, such a moiety in a linker does not connect two nucleosides.

In some embodiments, a linker has the structure of L. In some embodiments, a linker is bivalent. In some embodiments, a linker is polyvalent. In some embodiments, a linker can connect two or more additional chemical moieties to an oligonucleotide chain as described herein. For example, some embodiments, one or two or three or more additional chemical moieties, e.g., GalNAc moieties, are connected to an oligonucleotide chain (e.g., at 5'-end) through a multivalent linker moiety.

[00967] In some embodiments, an additional chemical moiety is cleaved from the remainder of an oligonucleotide, e.g., an oligonucleotide chain, e.g., after administration to a system, cell, tissue, organ, subject, etc. In some embodiments, additional chemical moieties promote, increase, and/or accelerate delivery to certain cells, and after delivery of oligonucleotides into such cells, additional chemical moieties are cleaved from oligonucleotides. In some embodiments, linker moieties comprise one or more cleavable moieties that can be cleaved at desirable locations (e.g., within certain type of cells, subcellular compartments such as lysosomes, etc.) and/or timing. In some embodiments, a cleavable moiety is selectively cleaved by a polypeptide, e.g., an enzyme such as a nuclease. Many useful cleavable moieties and cleavable linkers are reported and can be utilized in accordance with the present disclosure. In some embodiments, a cleavable moiety is or comprises one or more functional groups selected from amide, ester, ether, phosphodiester, disulfide, carbamate, etc. In some embodiments, a linker is as described in WO 2012/030683, WO 2021/030778, WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, or WO 2020/252376.

[00968] As described herein, in some embodiments, an additional chemical moiety, e.g., Mod001, may facilitate delivery of an oligonucleotide. In some embodiments, after delivery additional chemical moiety is cleaved. In some embodiments, additional moieties are released after delivery or administration, providing oligonucleotides to be delivered. In some embodiments, linkers (e.g., L001) for conjugating additional chemical moieties are cleaved. In some embodiments, an oligonucleotide has the structure of an oligonucleotide chain of an oligonucleotide comprising an additional chemical moiety and optionally a linker. In some embodiments, an oligonucleotide has the structure of a released oligonucleotide after an additional chemical moiety is cleaved from an oligonucleotide comprising an additional chemical moiety. In some embodiments, a linker, e.g., L001, is also cleaved from an oligonucleotide. In some embodiments, an oligonucleotide is formed by cleaving the additional chemical moiety from the oligonucleotide chain of an oligonucleotide comprising an additional chemical moiety. In some embodiments, an additional chemical moiety is cleaved after an oligonucleotide is delivered into a cell. In some embodiments, an additional chemical moiety is cleaved after an oligonucleotide is administered to a subject.

[00969] In some embodiments, the provided disclosure provides technologies for delivering an oligonucleotide, comprising administering a conjugate of the oligonucleotide, wherein the conjugate comprising the oligonucleotide to be delivered and an additional chemical moiety as described herein. In some embodiments, an oligonucleotide is conjugated with one or more additional chemical moieties independently and optionally through one or more linkers. In some embodiments, an oligonucleotide is conjugated with an

additional chemical moiety through a linker. For example, in some embodiments, an oligonucleotide comprising GalNAc in Table 1 or Table 1A (e.g., ADR-0111820) is administered, and the corresponding oligonucleotide without GalNAc (e.g., without the 5'-end p, [nC6o] and [GalNAc3C12oyl] (e.g., RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0)) is delivered. In some embodiments, the present disclosure provides an oligonucleotide, wherein the oligonucleotide is an oligonucleotide in Table 1 or Table 1A, but without the 5'-end p, [nC6o] and [GalNAc3C12oyl]. For example, in some embodiments, an oligonucleotide is an oligonucleotide selected from the Table below:

ID	HELM Description
ADR-0110420-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0110652-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0110667-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0110481-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0111148-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0111146-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0111820-B	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0
ADR-0111776-	RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)

B	p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

In some embodiments, an oligonucleotide is ADR-0110420-B. In some embodiments, an oligonucleotide is ADR-0110652-B. In some embodiments, an oligonucleotide is ADR-0110667-B. In some embodiments, an oligonucleotide is ADR-0110481-B. In some embodiments, an oligonucleotide is ADR-0111148-B. In some embodiments, an oligonucleotide is ADR-0111146-B. In some embodiments, an oligonucleotide is ADR-0111820-B. In some embodiments, an oligonucleotide is ADR-0111776-B. In some embodiments, such an oligonucleotide can be delivered by administering a corresponding conjugate oligonucleotide (e.g., a conjugate comprising a ASGPR ligand such as GalNAc). For example, in some embodiments, ADR-0110420-B, ADR-0110652-B, ADR-0110667-B, ADR-0110481-B, ADR-0111148-B, ADR-0111146-B, ADR-0111820-B, and ADR-0111776-B can be delivered by administering ADR-0110420, ADR-0110652, ADR-0110667, ADR-0110481, ADR-0111148, ADR-0111146, ADR-0111820, and ADR-0111776, respectively.

[00970] As demonstrated herein, provided technologies can provide high levels of activities and/or desired properties, in some embodiments, without utilizing particular structural elements (e.g., modifications, linkage configurations and/or patterns, etc.) reported to be desired and/or necessary (e.g., those reported in WO 2019/219581), though certain such structural elements may be incorporated into oligonucleotides in combination with various other structural elements in accordance with the present disclosure. For example, in some embodiments, oligonucleotides of the present disclosure have fewer nucleosides 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine), contain one or more phosphorothioate internucleotidic linkages at one or more positions where a phosphorothioate internucleotidic linkage was reportedly not favored or not allowed, contain one or more Sp phosphorothioate internucleotidic linkages at one or more positions where a Sp phosphorothioate internucleotidic linkage was reportedly not favored or not allowed, contain one or more Rp phosphorothioate internucleotidic linkages at one or more positions where a Rp phosphorothioate internucleotidic linkage was reportedly not favored or not allowed, and/or contain different modifications (e.g., internucleotidic linkage modifications, sugar modifications, etc.) and/or stereochemistry at one or more locations compared to those reportedly favorable or required for certain oligonucleotide properties and/or activities (e.g., presence of 2'-MOE, absence of phosphorothioate linkages at certain positions, absence of *S*p phosphorothioate linkages at certain positions, and/or absence of *R*p phosphorothioate linkages at certain positions were reportedly favorable or required for certain oligonucleotide properties and/or activities; as demonstrated herein, provided technologies can provide desired properties and/or high activities without utilizing 2'-MOE, without avoiding phosphorothioate linkages at one or more such certain positions, without avoiding *S*p phosphorothioate linkages at one or more such certain positions, and/or without avoiding *R*p phosphorothioate linkages at one or more such certain positions). Additionally or alternatively, provided oligonucleotides incorporates structural elements that were not previously recognized such as utilization of

certain modifications (e.g., base modifications, sugar modifications (e.g., 2'-F), linkage modifications (e.g., non-negatively charged internucleotidic linkages), additional moieties, etc.) and levels, patterns, and combinations thereof.

[00971] For example, in some embodiments, as described herein, provided oligonucleotides contain no more than 5, 6, 7, 8, 9, 10, 11 or 12 nucleosides 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine).

[00972] Alternatively or additionally, as described herein (e.g., illustrated in certain Examples), for structural elements 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine), in some embodiments, about 50%-100% (e.g., about or at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%) of internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a modified internucleotidic linkage, which is optionally chirally controlled. In some embodiments, no more than 1, 2, or 3 internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside are natural phosphate linkages. In some embodiments, no such internucleotidic linkage is natural phosphate linkages. In some embodiments, no more than 1 such internucleotidic linkage is natural phosphate linkages. In some embodiments, no more than 2 such internucleotidic linkages are natural phosphate linkages. In some embodiments, no more than 3 such internucleotidic linkages are natural phosphate linkages. In some embodiments, each modified internucleotidic linkage is independently a phosphorothioate or a non-negatively charged internucleotidic linkage (e.g., n001). In some embodiments, each phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, no more than 1, 2, or 3 internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside are *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage bonded to a nucleoside opposite to a target nucleoside at the 3'-position of its sugar (considered a -1 position) is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, it is the only *R*p phosphorothioate internucleotidic linkage 3' to a nucleoside opposite to a target nucleoside. In some embodiments, an internucleotidic linkage at position -3 relative to a nucleoside opposite to a target nucleoside (e.g., for $\ldots N_0N\text{-}_1N\text{-}_2N\text{-}_3\ldots$, the internucleotidic linkage linking $N\text{-}_2$ and $N\text{-}_3$ wherein N_0 is a nucleoside opposite to a target nucleoside) is not a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -6 relative to a nucleoside opposite to a target nucleoside is not a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position -4 and/or -5 relative to a nucleoside opposite to a target nucleoside is independently a modified internucleotidic linkage, e.g., a phosphorothioate internucleotidic linkage, or is independently a *R*p phosphorothioate internucleotidic linkage. In some embodiments, one or more or all internucleotidic linkages at positions -1, -3, -4, -5, and -6 are each independently a *S*p internucleotidic linkage. In some embodiments, one or more or all internucleotidic linkages at positions -1, -3, -4, -5, and -6 are each independently a *S*p phosphorothioate internucleotidic linkage. In some embodiments, internucleotidic linkage(s) at position(s) -4 and/or -5 are each independently a *R*p internucleotidic linkage. In some embodiments, internucleotidic linkage(s) at position(s) -4 and/or -5 are each independently a *R*p phosphorothioate internucleotidic linkage.

In many embodiments, no more than 1, 2, 3, 4, or 5 internucleotidic linkages are *R*p phosphorothioate internucleotidic linkage.

[00973] Alternatively or additionally, as described herein (e.g., illustrated in certain Examples), in some embodiments, about 50%-100% (e.g., about or at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%) of internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a modified internucleotidic linkage, which is optionally chirally controlled. In some embodiments, no or no more than 1, 2, or 3 internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are not modified internucleotidic linkages. In some embodiments, no or no more than 1, 2, or 3 internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are not phosphorothioate internucleotidic linkages. In some embodiments, no or no more than 1, 2, or 3 internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are not *S*p phosphorothioate internucleotidic linkages. In some embodiments, no more than 1, 2, or 3 internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are natural phosphate linkages. In some embodiments, no such internucleotidic linkage is natural phosphate linkages. In some embodiments, no more than 1 such internucleotidic linkage is natural phosphate linkages. In some embodiments, no more than 2 such internucleotidic linkages are natural phosphate linkages. In some embodiments, no more than 3 such internucleotidic linkages are natural phosphate linkages. In some embodiments, each modified internucleotidic linkage is independently a phosphorothioate or a non-negatively charged internucleotidic linkage (e.g., n001). In some embodiments, there are no 2, 3, or 4 consecutive internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside, each of which is not a phosphorothioate internucleotidic linkage. In some embodiments, there are no 2, 3, or 4 consecutive internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside, each of which is chirally controlled and is not a *S*p phosphorothioate internucleotidic linkage. In some embodiments, no or no more than 1, 2, 3, 4, or 5 internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage bonded to a nucleoside opposite to a target nucleoside at the 5'-position of its sugar (considered a +1 position) is a *R*p phosphorothioate internucleotidic linkage. In some embodiments, it is the only *R*p phosphorothioate internucleotidic linkage 3' to a nucleoside opposite to a target nucleoside. In some embodiments, an internucleotidic linkage at position +5 relative to a nucleoside opposite to a target nucleoside (e.g., for $\ldots N_{+5}N_{+4}N_{+3}N_{+2}N_{+1}N_0\ldots$, the internucleotidic linkage linking N_{+4} and N_{+5} wherein N_0 is a nucleoside opposite to a target nucleoside) is not a *R*p phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at positions +11 is not a *S*p phosphorothioate internucleotidic linkage. In some embodiments, one or more or all internucleotidic linkages at positions +6 to +8 relative to a nucleoside opposite to a target nucleoside are each independently a modified internucleotidic linkage, optionally chirally controlled. In some embodiments, each of them is independently a phosphorothioate internucleotidic linkage. In some embodiments, each of them is independently a *S*p phosphorothioate internucleotidic linkage. In some

embodiments, one or more or all internucleotidic linkages at positions +6 to +8 relative to a nucleoside opposite to a target nucleoside are each independently a phosphorothioate internucleotidic linkage, optionally chirally controlled. In some embodiments, one or more or all internucleotidic linkages at positions +6, +7, +8, +9, and +11 are each independently *Rp* internucleotidic linkages. In some embodiments, one or more or all internucleotidic linkages at positions +6, +7, +8, +9, and +11 are each independently *Rp* phosphorothioate internucleotidic linkages. In some embodiments, one or more or all internucleotidic linkages at positions +5, +6, +7, +8, and +9 relative to a nucleoside opposite to a target adenosine are each independently *Sp* internucleotidic linkages. In some embodiments, one or more or all internucleotidic linkages at positions +5, +6, +7, +8, and +9 relative to a nucleoside opposite to a target adenosine are each independently *Sp* phosphorothioate internucleotidic linkages. In some embodiments, an internucleotidic linkage at position +5 is a *Sp* internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +5 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +6 is a *Sp* internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +6 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +7 is a *Sp* internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +7 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +8 is a *Sp* internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +8 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +9 is a *Sp* internucleotidic linkage. In some embodiments, an internucleotidic linkage at position +9 is a *Sp* phosphorothioate internucleotidic linkage. In some embodiments, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32, or about 50%-100% (e.g., about or at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%) of internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently chirally controlled and a *Sp* internucleotidic linkage. In some embodiments, at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, or about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, or 32, or about 50%-100% (e.g., about or at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95%) of phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently chirally controlled and are *Sp*. In some embodiments, each phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) is chirally controlled. In some embodiments, each phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) is *Sp*.

[00974] Alternatively or additionally, as described herein (e.g., illustrated in certain Examples), in some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 15-40%, 20-30%, 25-30%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, of all internucleotidic linkages in an oligonucleotide are independently a natural phosphate linkage. In some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-

40%, 10-30%, 15-40%, 20-30%, 25-30%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, of all internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are independently a natural phosphate linkage. In some embodiments, one or more, e.g., about 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 5-6, 5-7, 5-8, 5-9, 5-10, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, internucleotidic linkages in an oligonucleotide are independently a natural phosphate linkage. In some embodiments, one or more, e.g., about 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 5-6, 5-7, 5-8, 5-9, 5-10, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are independently a natural phosphate linkage. In some embodiments, one or more internucleotidic linkages at one or more of positions +3 (between $N_{+4}N_{+3}$), +4, +6, +8, +9, +12, +14, +15, +17, and +18 are independently a natural phosphate linkage. In some embodiments, there are 4 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 5 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 6 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 7 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 8 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 9 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 10 natural phosphate linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, one or more internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a natural phosphate linkage. In some embodiments, there is one natural phosphate linkage 3' to a nucleoside opposite to a target nucleoside. In some embodiments, an internucleotidic linkage at position -3 is a natural phosphate linkage.

[00975] Alternatively or additionally, as described herein (e.g., illustrated in certain Examples), in some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 15-40%, 20-30%, 25-30%, 30%-70%, 40-70%, 40%-65%, 40%-60%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, or 65% of all internucleotidic linkages in an oligonucleotide are independently a phosphorothioate internucleotidic linkage. In some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 15-40%, 20-30%, 25-30%, 30%-70%, 40-70%, 40%-65%, 40%-60%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, or 65% of all internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are independently a natural phosphate linkage. In some embodiments, one or more, e.g., about 1-30, 1-25, 1-20, 1-15, 5-30, 5-25, 5-20, 5-15, 10-30, 10-25, 10-20, 10-15, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, internucleotidic linkages in an oligonucleotide are independently a phosphorothioate internucleotidic linkage. In some embodiments, one or more, e.g., about 1-30, 1-25, 1-20, 1-15, 5-30, 5-25, 5-20, 5-15, 10-30, 10-25, 10-20, 10-15, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30, internucleotidic linkages 5' to a nucleoside opposite

to a target nucleoside (e.g., a target adenosine) are independently a phosphorothioate internucleotidic linkage. In some embodiments, one or more internucleotidic linkages at one or more of positions +1 (between $N_{+1}N_0$), +2, +5, +6, +7, +8, +11, +14, +15, +16, +17, +19, +20, +21, and +22 are independently a phosphorothioate internucleotidic linkage. In some embodiments, there are 5 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 10 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 11 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 12 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 13 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 14 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 15 or more phosphorothioate internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, one or more internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a phosphorothioate internucleotidic linkage. In some embodiments, there is one phosphorothioate internucleotidic linkage 3' to a nucleoside opposite to a target nucleoside. In some embodiments, there are two phosphorothioate internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside. In some embodiments, there are three phosphorothioate internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside. In some embodiments, one or more or all internucleotidic linkages at positions -1, -4 and -5 are independently a phosphorothioate internucleotidic linkage. In some embodiments, each phosphorothioate internucleotidic linkage is independently chirally controlled. In some embodiments, about or at least about 80%, 85%, 90% or 95% of all phosphorothioate internucleotidic linkages are independently *Sp*. In some embodiments, each phosphorothioate internucleotidic linkage is independently *Sp*.

[00976] Alternatively or additionally, as described herein (e.g., illustrated in certain Examples), in some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 10%-20%, 10-15%, 15-40%, 15%-35%, 15%-30%, 15-25%, 15-20%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, of all internucleotidic linkages in an oligonucleotide are independently a non-negatively charged internucleotidic linkage. In some embodiments, about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 10%-20%, 10-15%, 15-40%, 15%-35%, 15%-30%, 15-25%, 15-20%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, of all internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a non-negatively charged internucleotidic linkage. In some embodiments, one or more, e.g., about 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 5-6, 5-7, 5-8, 5-9, 5-10, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, internucleotidic linkages in an oligonucleotide is independently a non-negatively charged internucleotidic linkage. In some embodiments, one or more, e.g., about 1-15, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 5-6, 5-7, 5-8, 5-9, 5-10, or about or at least about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, internucleotidic linkages

5' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) is independently a non-negatively charged internucleotidic linkage. In some embodiments, one or more internucleotidic linkages at one or more or all of positions +5 (between $N_{+5}N_{+4}$), +10, +13 or +23 are independently a non-negatively charged internucleotidic linkage. In some embodiments, there are 2 or more non-negatively charged internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 3 or more non-negatively charged internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 4 or more non-negatively charged internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, there are 5 or more non-negatively charged internucleotidic linkages 5' to a nucleoside opposite to a target nucleoside. In some embodiments, one or more internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside (e.g., a target adenosine) are each independently a non-negatively charged internucleotidic linkage. In some embodiments, there is one non-negatively charged internucleotidic linkage 3' to a nucleoside opposite to a target nucleoside. In some embodiments, there are two or more non-negatively charged internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside. In some embodiments, there are two non-negatively charged internucleotidic linkages 3' to a nucleoside opposite to a target nucleoside. In some embodiments, one or both internucleotidic linkages at positions -2 and -6 are independently a non-negatively charged internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is independently a neutral internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, each non-negatively charged internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage. In some embodiments, a non-negatively charged internucleotidic linkage is n001. In some embodiments, each non-negatively charged internucleotidic linkage is independently n001. In some embodiments, a non-negatively charged internucleotidic linkage is chirally controlled. In some embodiments, each non-negatively charged internucleotidic linkage is independently chirally controlled. In some embodiments, a non-negatively charged internucleotidic linkage is *R*p. In some embodiments, a non-negatively charged internucleotidic linkage is *S*p. In some embodiments, each non-negatively charged internucleotidic linkage is independently *S*p. In some embodiments, each n001 is independently *S*p except that each n001 bonded to 3'-carbon of dI is independently *R*p.

ADAR

[00977] Among other things, provided technologies can provide modification/editing of target adenosine by converting A to I. In some embodiments, oligonucleotides and/or duplexes formed by oligonucleotides with target nucleic acids interact with proteins, e.g., ADAR proteins. In some embodiments, such proteins comprise adenosine modifying activities and can modify target adenosine in target nucleic acids, e.g., converting them to inosine.

[00978] ADAR proteins are naturally expressed proteins in various cells, tissues, organs and/or organism. It has been reported that some ADAR proteins, e.g., ADAR1 and ADAR2, can edit adenosine through

deamination, converting adenosine to inosine which can provide a number of functions including being read as or similar to G during translation. Mechanism of ADAR-mediated mRNA editing (e.g., deamination) has been reported. For example, ADAR proteins are reported to catalyze conversion of adenosine to inosine on double-stranded RNA substrates with mismatches. As appreciated by those skilled in the art, inosine can be recognized as guanosine by cellular translation and/or splicing machinery. ADAR can thus be used for functional adenosine to guanosine editing of nucleic acids, e.g., pre-mRNA and mRNA substrates.

[00979] In some embodiments, the present disclosure provides oligonucleotides and compositions thereof for ADAR-mediated editing of target adenosine in target nucleic acids, e.g. RNA. ADAR-mediated RNA-editing can offer several advantages over DNA-editing, e.g., delivery is simplified as expression of recombinant proteins like Cas9 is not required. Both ADAR1 and ADAR2 are endogenous enzymes, so cellular delivery of oligonucleotides alone can be sufficient for editing. Off-target effects, if any, are transient and changes are not made to genomic DNA. Additionally, ADAR-mediated editing can be used in post-mitotic cells and it does not require an HDR-template for repair. Three vertebrate ADAR genes have been reported with common functional domains (Nishikura Nat Rev Mol Cell Biol. 2016 Feb; 17(2): 83–96.; Nishikura Annu Rev Biochem. 2010; 79: 321–349.; Thomas and Beal Bioessays. 2017 Apr;39(4)). All 3 ADARs contain a dsRNA-binding domains (dsRBD), which can contact dsRNA substrates. Some ADAR1 also contains Z-DNA-binding domains. ADAR1 has been reported to expressed significantly in brain, lung, kidney, liver, and heart, etc., and may occur in two isoforms. In some embodiments, isoform p150 can be induced by interferon while isoform p110 can be constitutively expressed. In some embodiments, it can be beneficial to utilize p110 as it is reported to be ubiquitously and constitutively expressed. ADAR2 can be highly expressed, e.g. in the brain and lungs, and is reported to be exclusively localized to the nucleus. ADAR3 is reported to be catalytically inactive and expressed only in the brain. Potential differences in tissue expression can be taken into consideration when choosing a therapeutic target.

[00980] Use of oligonucleotides for RNA editing by ADAR has been reported. Among other things, the present disclosure recognizes that previously reported technologies generally suffer one or more disadvantages, such as low stability (e.g., oligonucleotides with natural RNA sugars), low editing efficiency, low editing specificity (e.g., a number of As are edited in a portion of a target nucleic acid substantially complementary to an oligonucleotide), specific structures in oligonucleotides for ADAR recognition/recruitment, exogenous proteins (e.g.,, those engineered to recognize oligonucleotides with specific structures and/or duplexes thereof (e.g.,, with target nucleic acids) for editing), etc. Additionally, previously reported technologies typically utilize stereorandom oligonucleotide compositions when oligonucleotides comprise one or more chiral linkage phosphorus of modified internucleotidic linkages.

[00981] For example, various reported oligonucleotides contain ADAR-recruiting domains. Merkle et al., Nat Biotechnol. 2019 Feb;37(2):133-138disclosed oligonucleotides comprising an imperfect 20-bp hairpin ADAR-recruiting domain that is an intramolecular stem loop to recruit endogenous human ADAR2 to edit endogenous transcript. Oligonucleotides reported in Mali et al., Nat Methods. 2019 Mar;16(3):239-242contain

ADAR substrate GluR2 pre-messenger RNA sequences or MS2 hairpins in addition to specificity domains that hybridize to the target mRNA.

[00982] Certain reported editing approach utilizes exogenous or engineered proteins, e.g.,, those utilizing CRISPR/Cas9 system. For example, Komor et al. Nature 2016 volume533, pages420–424 disclosed deaminase coupled with CRISPR-Cas9 to create programmable DNA base editors. Since it engages in exogenous editing proteins, it requires the delivery of both the CRISPR/Cas9 system and the guide RNA.

[00983] Among other things, the present disclosure provides technologies comprising one or more features such as sugar modifications, base modifications, internucleotidic linkage modifications, control of stereochemistry, various patterns thereof, etc. to solve one or more or all disadvantaged suffered from prior adenosine editing technologies, for example, through providing chirally controlled oligonucleotide compositions of designed oligonucleotides described herein. For example, as demonstrated herein, ADAR-recruiting loops are optional and not required for provided technology.

[00984] As appreciated by those skilled in the art, one or more of such useful features may be utilized to improve oligonucleotides in prior technologies (e.g., those described in WO 2016097212, WO 2017220751, WO 2018041973, WO 2018134301, oligonucleotides and oligonucleotide compositions of each of which are independently incorporated by reference). In some embodiments, the present disclosure provides improvements of prior technologies by apply one or more useful features described herein to prior reported oligonucleotide base sequences. In some embodiments, the present disclosure provides chirally controlled oligonucleotide compositions of previously reported oligonucleotides that may be useful for adenosine editing. In some embodiments, the present disclosure provides improvements of previously reported adenosine editing using stereorandom oligonucleotide compositions by performing such editing using chirally controlled oligonucleotide compositions.

[00985] As reported, ADAR proteins may have various isoforms. For example, ADAR1 has, among others, a reported p110 isoform and a reported p150 isoform. In some embodiments, it was observed that certain chirally controlled oligonucleotide compositions can provide high levels of adenosine modification (e.g., conversion of A to I) with multiple isoforms, in some embodiments, both p110 and p150 isoforms, while stereorandom compositions provide low levels of adenosine modification for one or more isoforms (e.g., p110). In some embodiments, chirally controlled oligonucleotide composition are particularly useful for adenosine modification in systems (e.g., cells, tissues, organs, organisms, subjects, etc.) expressing or comprising the p110 isoform of ADAR1, particularly those expressing or comprising high levels of the p110 isoform of ADAR1 relative to the p150 isoform, or those expressing no or low levels of ADAR1 p150.

[00986] In some embodiments, the present disclosure provides Cis-acting (CisA) oligonucleotide that do not require stem loop in the structure. In some embodiments, a provided oligonucleotide can form a dsRNA structure with a target mRNA through base pairing. In some embodiments, formed dsRNA structures (optionally with secondary mismatches) contain bulges that promote ADAR binding and therefore, can facilitate ADAR-mediated editing (e.g., deamination of a target adenosine). In some embodiments,

oligonucleotides of the present disclosure are shorter than LSL oligonucleotides or CSL oligonucleotides, e.g., no more than or about 32 nt, no more than or about 31 nt, no more than or about 30 nt, no more than or about 29 nt, no more than or about 28 nt, no more than or about 27 nt, or no more than or about 26 nt in length, and can provide high editing efficiency.

Duplexing and Targeting Regions

[00987] In some embodiments, the present disclosure provides an oligonucleotide comprising:

a duplexing region; and

a targeting region;

wherein:

a duplexing region is capable of forming a duplex with a nucleic acid; and

a targeting region is capable of forming a duplex with a target nucleic acid comprising a target adenosine.

[00988] In some embodiments, a duplexing region is or comprises a first domain as described herein. In some embodiments, a targeting region is or comprises a second domain as described herein.

[00989] In some embodiments, a duplexing region is capable of forming a duplex with a nucleic acid, wherein the nucleic acid is not a target nucleic acid. In some embodiments, a duplexing region forms a duplex with a target nucleic acid. In some embodiments, a duplexing region forms a duplex with a nucleic acid expressed in a system, e.g., a cell. In some embodiments, a duplexing region forms a duplex with an exogenous nucleic acid, e.g., an oligonucleotide. In some embodiments, a duplexing region forms a duplex with a nucleic acid which is or comprises a RNA portion. In some embodiments, a duplex formed can be recognized by a polypeptide such as an ADAR polypeptide, e.g., ADAR1 (p110 or p150 or both), ADAR2, etc. In some embodiments, a duplex formed can recruit a polypeptide such as an ADAR polypeptide, e.g., ADAR1 (p110 or p150 or both), ADAR2, etc. In some embodiments, a duplex formed recruit ADAR1. In some embodiments, a duplex formed recruit ADAR1 p110. In some embodiments, a duplex formed recruit ADAR1 p150. In some embodiments, a duplex formed recruit ADAR2. In some embodiments, a duplex formed recruit ADAR1 p110 and p150. In some embodiments, a duplex formed recruit ADAR1 and ADAR2. In some embodiments, a duplex formed recruit ADAR1 p110, ADAR p150 and/or ADAR2. In some embodiments, a duplex formed recruit ADAR1 p110 and p150 and ADAR2.

[00990] In some embodiments, a duplexing region forms a duplex with an oligonucleotide (which oligonucleotide may be referred to as "a duplexing oligonucleotide"). In some embodiments, a duplexing oligonucleotide comprises one or more modified nucleobases, modified sugars and/or modified internucleotidic linkages. In some embodiments, an duplexing oligonucleotide comprises a duplex-forming region that is complementary to a duplexing region. As those skilled in the art appreciate, in many instances, perfect complementary is not required and one or more wobbles, bulges, mismatches, etc. may be well tolerated. For example, ADAR proteins have been reported to bind to and/or utilize as substrates both perfectly and imperfectly complementary duplexes.

[00991] Duplexing regions and/or duplexing-forming regions can be of various lengths. In some embodiments, they are at least 10 (e.g., about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, about 10-20, 10-25, 10-30, 10-40, 10-50, 10-100, 14-20, 14-25, 14-30, 14-40, 14-50, 14-100, 15-20, 15-25, 15-30, 15-40, 15-50, 15-100, 16-20, 16-25, 16-30, 16-40, 16-50, 16-100, 17-20, 17-25, 17-30, 17-40, 17-50, 17-100, 18-20, 18-25, 18-30, 18-40, 18-50, 18-100, 19-20, 19-25, 19-30, 19-40, 19-50, 19-100, 20-25, 20-30, 20-40, 20-50, 20-100, etc.) nucleosides in length. In some embodiments, a length is about or at least about 10 nucleosides in length. In some embodiments, a length is about or at least about 11 nucleosides in length. In some embodiments, a length is about or at least about 12 nucleosides in length. In some embodiments, a length is about or at least about 13 nucleosides in length. In some embodiments, a length is about or at least about 14 nucleosides in length. In some embodiments, a length is about or at least about 15 nucleosides in length. In some embodiments, a length is about or at least about 16 nucleosides in length. In some embodiments, a length is about or at least about 17 nucleosides in length. In some embodiments, a length is about or at least about 18 nucleosides in length. In some embodiments, a length is about or at least about 19 nucleosides in length. In some embodiments, a length is about or at least about 20 nucleosides in length.

[00992] In some embodiments, a duplexing oligonucleotide consists of or consists essentially of a duplex-forming region. In some embodiments, a duplexing oligonucleotide further comprises one or more additional regions in addition to a duplex-forming region. In some embodiments, a duplexing oligonucleotide comprises a stem-loop region. In some embodiments, a duplexing oligonucleotide comprises or consists of a duplex-forming region and a stem-loop region. In some embodiments, a stem region is about or at least about 2, 3, 4, 5, 6, 7, 8, 9, or 10 (e.g., about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, about 4-10, 4-15, 4-20, 4-25, 4-30, 4-40, 4-50, 5-10, 5-15, 5-20, 5-25, 5-30, 5-40, 5-50, 6-10, 6-15, 6-20, 6-25, 6-30, 6-40, 6-50, 7-10, 7-15, 7-20, 7-25, 7-30, 7-40, 7-50, 8-10, 8-15, 8-20, 8-25, 8-30, 8-40, 8-50, 9-10, 9-15, 9-20, 9-25, 9-30, 9-40, 9-50, 10-15, 10-25, 10-30, 10-40, 10-50, 10-100, etc.) nucleobase in length. In some embodiments, it is about or at least about 5 nucleobases in length. In some embodiments, it is about or at least about 6 nucleobases in length. In some embodiments, it is about or at least about 7 nucleobases in length. In some embodiments, it is about or at least about 8 nucleobases in length. In some embodiments, it is about or at least about 9 nucleobases in length. In some embodiments, it is about or at least about 10 nucleobases in length.

[00993] In some embodiments, one or more additional regions may promote, encourage, facilitate and/or contribute recruitment of and/or recognition by and/or interaction with a polypeptide, e.g., ADAR1 (p110 and/or p150) and/or ADAR2. In some embodiments, for duplexing oligonucleotides comprising one or more additional regions, shorter duplex-forming regions may be utilized compared to absence of such additional regions.

[00994] In some embodiments, a duplex structure formed by a duplex region and a duplexing oligonucleotide can recruit a polypeptide, e.g., ADAR1 (p110 and/or p150) and/or ADAR2. In some

embodiments, a duplex structure is or comprises a recruiting portion as described in WO 2016/097212.

[00995] In some embodiments, a duplexing oligonucleotide comprises one or more sugar, nucleobase, and/or internucleotidic linkage modifications as described herein. In some embodiments, a duplexing oligonucleotide comprises one or more sugar modification. In some embodiments, a majority, as described herein, of, or all of, the sugars in a duplexing oligonucleotide is a modified sugar. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, each modified sugar is independently a 2'-modified sugar. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is not hydrogen. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-F modified sugar. In some embodiments, a duplexing oligonucleotide comprises one or more modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages. In some embodiments, a majority, as described herein, of or all of internucleotidic linkages of a duplexing oligonucleotide are independently modified internucleotidic linkages. In some embodiments, each internucleotidic linkage of a duplexing oligonucleotide is independently a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is n001. In some embodiments, each modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, a phosphorothioate internucleotidic linkage is not chirally controlled. In some embodiments, a majority, as described herein, of, or all of, chirally controlled phosphorothioate internucleotidic linkages are independently *Sp*. In some embodiments, all phosphorothioate internucleotidic linkages are *Sp*. In some embodiments, a duplexing oligonucleotide comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more) natural phosphate linkages. In some embodiments, when an oligonucleotide comprises one or more natural phosphate linkages, one or several internucleotidic linkages at the 5' and/or 3' end are independently modified internucleotidic linkages as described herein. In some embodiments, several internucleotidic linkages at both the 5' and 3' ends are independently modified internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic

linkages at the 5' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 3' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, increasing the number of modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages, etc., can increase editing efficiency, e.g., when more natural DNA/RNA sugars, 2'-F modified sugars, etc., are bonded to modified internucleotidic linkages such as phosphorothioate internucleotidic linkages.

[00996] In some embodiments, a duplexing region comprises one or more sugar, nucleobase and/or internucleotidic linkage modifications as described herein. In some embodiments, a duplexing region comprises one or more (e.g., 1-30, 1-20, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, etc.) modified sugars as described herein. In some embodiments, a majority, as described herein, of or all of sugars in a duplexing region are each independently a modified sugar as described herein. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, each modified sugar is independently a 2'-modified sugar. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is not hydrogen. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-F modified sugar. In some embodiments, about 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more of sugars in a duplexing region are each independently a 2'-F modified sugar. In some embodiments, as described herein, one or more sugars at an end of an oligonucleotide is independently a modified sugar. In some embodiments, as described herein, one or more sugars at an end of an oligonucleotide is independently a bicyclic sugar or a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, as described herein, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at an end of an oligonucleotide are each independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at both ends of an oligonucleotide are each independently a modified sugar; for example, in some oligonucleotides, 3 or more sugars at the 5' end are 2'-OMe modified sugars, and 4 or more sugars at the 3' end are 2'-OMe modified sugars. In some embodiments, a duplexing region comprises one or more (e.g., 1-30, 1-20, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, etc.) modified internucleotidic linkages as described herein. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages

at the 5' and/or 3' ends of an oligonucleotide are each independently a modified internucleotidic linkage, e.g., in some embodiments, each independently selected from a non-negatively charged internucleotidic linkage, a neutral internucleotidic linkage, a phosphoryl guanidine internucleotidic linkage, n001 and a phosphorothioate internucleotidic linkage. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 5' end of an oligonucleotide are each independently a modified internucleotidic linkage, and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 3' end of an oligonucleotide are each independently a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is n001. In some embodiments, each modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, a phosphorothioate internucleotidic linkage is not chirally controlled. In some embodiments, a majority, as described herein, of, or all of, chirally controlled phosphorothioate internucleotidic linkages are independently *Sp*. In some embodiments, all phosphorothioate internucleotidic linkages are *Sp*. In some embodiments, chiral modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages, are not chirally controlled. In some embodiments, a duplexing region comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more) natural phosphate linkages. In some embodiments, when an oligonucleotide comprises one or more natural phosphate linkages, one or several internucleotidic linkages at the 5' and/or 3' end are independently modified internucleotidic linkages as described herein. In some embodiments, several internucleotidic linkages at both the 5' and 3' ends are independently modified internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 5' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 3' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, incorporation of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) natural phosphate linkages at duplexing regions increase editing efficiency. In some embodiments, a majority of internucleotidic linkages (e.g., 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more) in a duplexing region are independently natural phosphate linkages. In some embodiments, except the one or more natural phosphate linkages at an end of an oligonucleotide (if any), each other internucleotidic linkage in a duplexing region is independently a natural phosphate linkage.

[00997] In some embodiments, a targeting region is or comprises an editing region as described herein. In some embodiments, a targeting region comprises 5'-$N_1N_0N_{-1}$-3' as described herein.

[00998] In some embodiments, a targeting region comprises one or more sugar, nucleobase and/or internucleotidic linkage modifications as described herein. In some embodiments, a targeting region comprises one or more (e.g., 1-30, 1-20, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, etc.) modified sugars as described herein. In some embodiments, a majority, as described herein, of or all of sugars in a targeting region are each independently a modified sugar as described herein. In some embodiments, a modified sugar is a 2'-modified sugar. In some embodiments, each modified sugar is independently a 2'-modified sugar. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is not hydrogen. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar, a bicyclic sugar, or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each modified sugar is independently selected from a 2'-F modified sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe or a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-OMe modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-MOE modified sugar. In some embodiments, each 2'-OR modified sugar is independently a 2'-F modified sugar. In some embodiments, about 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more of sugars in a targeting region are each independently a bicyclic sugar or a 2'-OR modified sugar wherein R is not hydrogen. In some embodiments, about 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more of sugars in a targeting region are each independently a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, about 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more of sugars in a targeting region are each independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in a targeting region except the sugars in an editing region is independently a modified sugar as described herein. In some embodiments, each sugar in a targeting region except the sugars in an editing region is independently a bicyclic sugar or a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a targeting region except the sugars in an editing region is independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic. In some embodiments, each sugar in a targeting region except the sugars in an editing region is independently a 2'-OMe or 2'-MOE modified sugar. In some embodiments, each sugar in a targeting region except the sugars in an editing region is independently a 2'-OMe modified sugar. In some embodiments, an editing region comprises or consists of three nucleosides wherein a nucleoside opposite to a target adenosine is in the middle of the three. In some embodiments, an editing region consists of three nucleosides wherein a nucleoside

opposite to a target adenosine is in the middle of the three. In some embodiments, an editing region comprising or consisting of 5'-$N_1N_0N_{-1}$-3'. In some embodiments, as described herein, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at an end of an oligonucleotide is independently a modified sugar. In some embodiments, as described herein, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at an end of an oligonucleotide is independently a bicyclic sugar or a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, as described herein, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at an end of an oligonucleotide are each independently a 2'-OR modified sugar wherein R is C_{1-6} aliphatic. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) sugars at both ends of an oligonucleotide are each independently a modified sugar; for example, in some oligonucleotides, 3 or more sugars at the 5' end are 2'-OMe modified sugars, and 4 or more sugars at the 3' end are 2'-OMe modified sugars. In some embodiments, a targeting region comprises one or more (e.g., 1-30, 1-20, 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more, etc.) modified internucleotidic linkages as described herein. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 5' and/or 3' ends of an oligonucleotide are each independently a modified internucleotidic linkage, e.g., in some embodiments, each independently selected from a non-negatively charged internucleotidic linkage, a neutral internucleotidic linkage, a phosphoryl guanidine internucleotidic linkage, n001 and a phosphorothioate internucleotidic linkage. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 5' end of an oligonucleotide are each independently a modified internucleotidic linkage, and one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 3' end of an oligonucleotide are each independently a modified internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a non-negatively charged internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a neutral internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage. In some embodiments, a modified internucleotidic linkage is n001. In some embodiments, each modified internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, each internucleotidic linkage is a phosphorothioate internucleotidic linkage. In some embodiments, a phosphorothioate internucleotidic linkage is chirally controlled. In some embodiments, a phosphorothioate internucleotidic linkage is not chirally controlled. In some embodiments, a majority, as described herein, of, or all of, chirally controlled phosphorothioate internucleotidic linkages are independently *Sp*. In some embodiments, all phosphorothioate internucleotidic linkages are *Sp*. In some embodiments, chiral modified internucleotidic linkages, e.g., phosphorothioate internucleotidic linkages, are not chirally controlled. In some embodiments, a targeting region comprises one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more) natural phosphate linkages. In some embodiments, when an oligonucleotide comprises one or more natural phosphate linkages, one or several internucleotidic linkages at the 5' and/or 3' end are independently modified

internucleotidic linkages as described herein. In some embodiments, several internucleotidic linkages at both the 5' and 3' ends are independently modified internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 5' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) internucleotidic linkages at the 3' end are modified internucleotidic linkages as described herein, e.g., phosphorothioate internucleotidic linkages. In some embodiments, incorporation of one or more (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 2-20, 2-10, 2-5, 3-5, etc.) natural phosphate linkages at targeting regions increase editing efficiency. In some embodiments, a majority of internucleotidic linkages (e.g., 50%-100%, 60%-100%, 70%-100%, 50%-90%, 50%-80%, 60%-90%, 60%-80%, 70%-90%, 70%-80%, or about or at least about 60%, 70%, 75%, 80%, 85%, 90%, 95% or more) in a targeting region are independently natural phosphate linkages. In some embodiments, except the one or more natural phosphate linkages at an end of an oligonucleotide (if any), each other internucleotidic linkage in a targeting region is independently a natural phosphate linkage.

[00999] In some embodiments, a targeting region is complementary to a sequence in a target nucleic acid. In some embodiments, a nucleic acid is or comprise RNA. In some embodiments, a nucleic acid is RNA. In some embodiments, a sequence in a target nucleic acid to which a target region is complementary to comprises a target adenosine. As those skilled in the art appreciate, full complementarity in many instances are not required, and one or more wobbles, bulges, mismatches, etc. may be present.

[01000] Targeting regions can be of various lengths. In some embodiments, a targeting region is at least 10 (e.g., about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more, about 10-20, 10-25, 10-30, 10-40, 10-50, 10-100, 14-20, 14-25, 14-30, 14-40, 14-50, 14-100, 15-20, 15-25, 15-30, 15-40, 15-50, 15-100, 16-20, 16-25, 16-30, 16-40, 16-50, 16-100, 17-20, 17-25, 17-30, 17-40, 17-50, 17-100, 18-20, 18-25, 18-30, 18-40, 18-50, 18-100, 19-20, 19-25, 19-30, 19-40, 19-50, 19-100, 20-25, 20-30, 20-40, 20-50, 20-100, etc.) nucleosides in length. In some embodiments, a length is about or at least about 10 nucleosides in length. In some embodiments, a length is about or at least about 11 nucleosides in length. In some embodiments, a length is about or at least about 12 nucleosides in length. In some embodiments, a length is about or at least about 13 nucleosides in length. In some embodiments, a length is about or at least about 14 nucleosides in length. In some embodiments, a length is about or at least about 15 nucleosides in length. In some embodiments, a length is about or at least about 16 nucleosides in length. In some embodiments, a length is about or at least about 17 nucleosides in length. In some embodiments, a length is about or at least about 18 nucleosides in length. In some embodiments, a length is about or at least about 19 nucleosides in length. In some embodiments, a length is about or at least about 20 nucleosides in length. In some embodiments, a length is about or at least about 21 nucleosides in length. In some embodiments, a length is about or at least about 22 nucleosides in length. In some embodiments, a length is about or at least about 23 nucleosides in length. In some embodiments, a length is about or at least about 24 nucleosides in length. In some embodiments, a length is about or at least about 25 nucleosides in length.

[01001] In some embodiments, an oligonucleotide comprises a targeting region and a duplexing region, wherein the targeting region is at the 3' side of the duplexing region. In some embodiments, an oligonucleotide comprises a targeting region and a duplexing region, wherein the targeting region is at the 5' side of the duplexing region. In some embodiments, an oligonucleotide consists of a targeting region and a duplexing region, wherein the targeting region is at the 3' side of the duplexing region. In some embodiments, an oligonucleotide consists of a targeting region and a duplexing region, wherein the targeting region is at the 5' side of the duplexing region. In some embodiments, an oligonucleotide comprise a targeting region, a duplexing region and a linker region between the target and duplexing regions. In some embodiments, a linker region comprises or is an oligonucleotide moiety.

[01002] In some embodiments, oligonucleotides comprising duplexing and targeting regions form complexes including duplexes with other nucleic acids e.g., duplexing oligonucleotides. In some embodiments, the present disclosure provides duplexes comprising oligonucleotides comprising duplexing and targeting regions and nucleic acids that form duplexes with duplexing regions. In some embodiments, the present disclosure provides duplexes comprising oligonucleotides comprising duplexing and targeting regions and duplexing oligonucleotides. In some embodiments, chirally controlled oligonucleotide compositions of oligonucleotides comprising duplexing and targeting regions are utilized (e.g., WV-42707). In some embodiments, non-chirally controlled oligonucleotide compositions of oligonucleotides comprising duplexing and targeting regions are utilized. In some embodiments, chirally controlled oligonucleotide compositions of duplexing oligonucleotides are utilized (e.g., WV-42724). In some embodiments, non-chirally controlled oligonucleotide compositions of duplexing oligonucleotides are utilized (e.g., WV-42721).

[01003] In some embodiments, duplexes are formed before administration. In some embodiments, oligonucleotides comprising duplexing and targeting regions and nucleic acids forming duplexes therewith (which may be referred to as "duplexing nucleic acids") are administered separately. In some embodiments, oligonucleotides comprising duplexing and targeting regions are administered prior to, concurrently with (either in a single or multiple compositions) or subsequently to duplexing nucleic acids (e.g., various duplexing oligonucleotides described herein). In some embodiments, duplexing nucleic acids are present in and/or can be expressed in cells and thus may not need to be administered directly.

[01004] Certain oligonucleotides comprising duplexing and targeting regions and/or duplexing nucleic acids (e.g., duplexing oligonucleotides) and/or uses are described herein.

[01005] In some embodiments, a target nucleic acid is or comprises RNA. In some embodiments, a target nucleic acid is or comprises mRNA. In some embodiments, a target adenosine in a target nucleic acid is edited to I.

Production of Oligonucleotides and Compositions

[01006] Various methods can be utilized for production of oligonucleotides and compositions and can be utilized in accordance with the present disclosure. For example, traditional phosphoramidite chemistry (e.g., phosphoramidites comprising $-CH_2CH_2CN$ and $-N(i\text{-}Pr)_2$) can be utilized to prepare stereorandom

oligonucleotides and compositions, and certain reagents and chirally controlled technologies can be utilized to prepare chirally controlled oligonucleotide compositions, e.g., as described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159.

[01007] In some embodiments, chirally controlled/stereoselective preparation of oligonucleotides and compositions thereof comprise utilization of a chiral auxiliary, e.g., as part of monomers, dimers (e.g., chirally pure dimers from separation), monomeric phosphoramidites, dimeric phosphoramidites (e.g., chirally pure dimers from separation), etc. Examples of such chiral auxiliary reagents, monomers, dimers, and phosphoramidites are described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the chiral auxiliary reagents, monomers, dimers, and phosphoramidites of each of which are independently incorporated herein by reference. In some embodiments, a chiral auxiliary is a chiral auxiliary described in any of: WO 2018/022473, WO 2018/098264, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159, the chiral auxiliaries of each of which are independently incorporated herein by reference.

[01008] In some embodiments, chirally controlled preparation technologies, including oligonucleotide synthesis cycles, reagents and conditions are described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, and/WO 2018/098264, WO 2018/022473, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/032612, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2018/223056, WO 2018/223073, WO 2018/223081, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159.

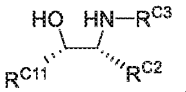
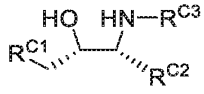
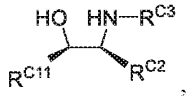
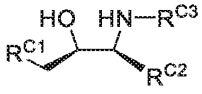
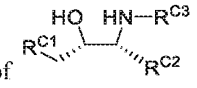
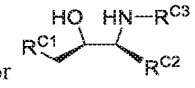
[01009] Once synthesized, provided oligonucleotides and compositions are typically further purified. Suitable purification technologies are widely known and practiced by those skilled in the art, including but not limited to those described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, and/or WO 2022/099159.

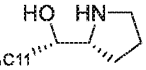
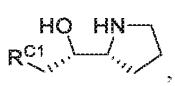
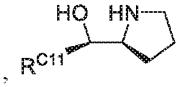
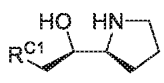
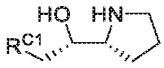
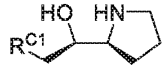
[01010] In some embodiments, a cycle comprises or consists of coupling, capping, modification and

deblocking. In some embodiments, a cycle comprises or consists of coupling, capping, modification, capping and deblocking. These steps are typically performed in the order they are listed, but in some embodiments, as appreciated by those skilled in the art, the order of certain steps, e.g., capping and modification, may be altered. If desired, one or more steps may be repeated to improve conversion, yield and/or purity as those skilled in the art often perform in syntheses. For example, in some embodiments, coupling may be repeated; in some embodiments, modification (e.g., oxidation to install =O, sulfurization to install =S, etc.) may be repeated; in some embodiments, coupling is repeated after modification which can convert a P(III) linkage to a P(V) linkage which can be more stable under certain circumstances, and coupling is routinely followed by modification to convert newly formed P(III) linkages to P(V) linkages. In some embodiments, when steps are repeated, different conditions may be employed (e.g., concentration, temperature, reagent, time, etc.).

[01011] Technologies for formulating provided oligonucleotides and/or preparing pharmaceutical compositions, e.g., for administration to subjects via various routes, are readily available in the art and can be utilized in accordance with the present disclosure, e.g., those described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, or WO 2018/237194 and references cited therein.

[01012] Technologies for formulating provided oligonucleotides and/or preparing pharmaceutical compositions, e.g., for administration to subjects via various routes, are readily available in the art and can be utilized in accordance with the present disclosure, e.g., those described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, or WO 2018/237194 and references cited therein.

[01013] In some embodiments, a useful chiral auxiliary has the structure of , , , or , or a salt thereof, wherein R^{C11} is $-L^{C1}-R^{C1}$, L^{C1} is optionally substituted $-CH_2-$, R^{C1} is R, $-Si(R)_3$, $-SO_2R$ or an electron-withdrawing group, and R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 3-10 membered saturated ring having, in addition to the nitrogen atom, 0-2 heteroatoms. In some embodiments, a useful chiral auxiliary has the structure of  or , wherein R^{C1} is R, $-Si(R)_3$ or $-SO_2R$, and R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 3-7 membered saturated ring having, in addition to the nitrogen atom, 0-2 heteroatoms. is a formed ring is an optionally substituted 5-

membered ring. In some embodiments, a useful chiral auxiliary has the structure of , ,  or , or a salt thereof. In some embodiments, a useful chiral auxiliary has the structure of  or . In some embodiments, a useful chiral auxiliary is a DPSE chiral auxiliary. In some embodiments, purity or stereochemical purity of a chiral auxiliary is at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, it is at least 85%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%. In some embodiments, it is at least 96%. In some embodiments, it is at least 97%. In some embodiments, it is at least 98%. In some embodiments, it is at least 99%.

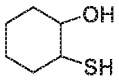
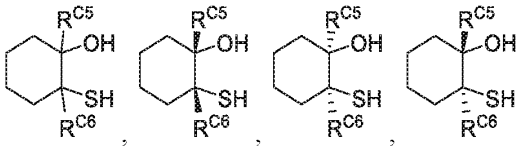
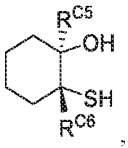
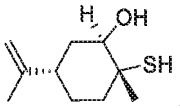
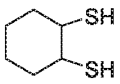
[01014] In some embodiments, L^{C1} is $-CH_2-$. In some embodiments, L^{C1} is substituted $-CH_2-$. In some embodiments, L^{C1} is mono-substituted $-CH_2-$.

[01015] In some embodiments, R^{C1} is R. In some embodiments, R^{C1} is optionally substituted phenyl. In some embodiments, R^{C1} is $-SiR_3$. In some embodiments, R^{C1} is $-SiPh_2Me$. In some embodiments, R^{C1} is $-SO_2R$. In some embodiments, R is not hydrogen. In some embodiments, R is optionally substituted phenyl. In some embodiments, R is phenyl. In some embodiments, R is optionally substituted C_{1-6} aliphatic. In some embodiments, R is C_{1-6} alkyl. In some embodiments, R is methyl. In some embodiments, R is t-butyl.

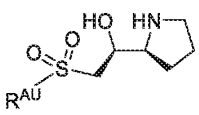
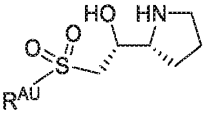
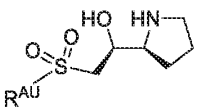
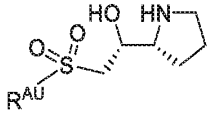
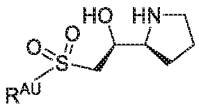
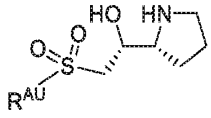
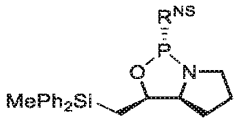
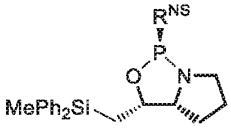
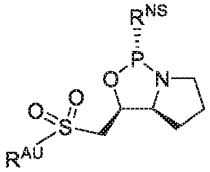
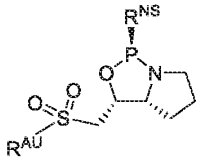
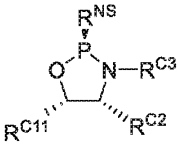
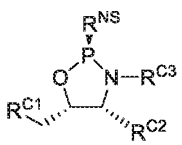
[01016] In some embodiments, R^{C1} is an electron-withdrawing group, such as $-C(O)R$, $-OP(O)(OR)_2$, $-OP(O)(R)_2$, $-P(O)(R)_2$, $-S(O)R$, $-S(O)_2R$, etc. In some embodiments, chiral auxiliaries comprising electron-withdrawing group R^{C1} groups are particularly useful for preparing chirally controlled non-negatively charged internucleotidic linkages and/or chirally controlled internucleotidic linkages bonded to natural RNA sugar.

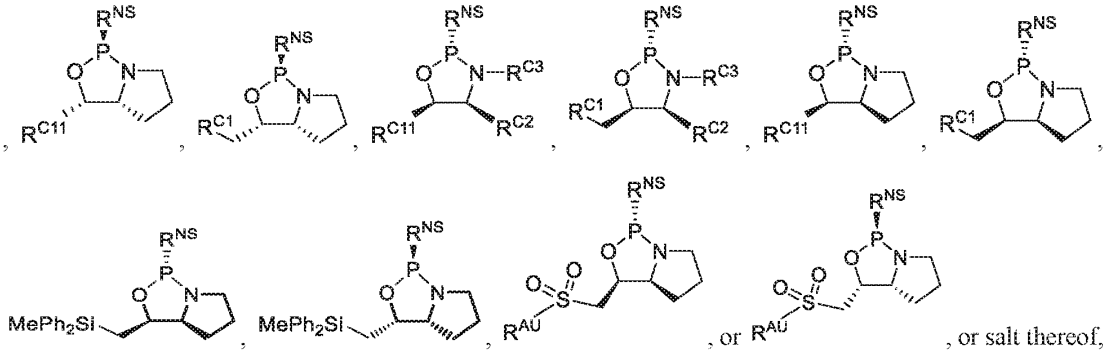
[01017] In some embodiments, R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 3-10 (e.g., 3, 4, 5, 6, 7, 8, 9, or 10) membered saturated ring having no heteroatoms in addition to the nitrogen atom. In some embodiments, R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 5-membered saturated ring having no heteroatoms in addition to the nitrogen atom.

[01018] In some embodiments, a compound has the structure of $H-X^C-C(R^{C5})_2-C(R^{C6})_2-SH$ or a salt thereof, wherein X^C is O or S, and each of R^{C5} and R^{C6} is independently R as described herein. In some embodiments, such a compound is useful for preparing a monomer. In some embodiments, such a compound is useful as a chiral auxiliary. In some embodiments, such a compound is particularly useful for preparing monomer which when utilized in oligonucleotide synthesis form bonds between their nitrogen atoms with linkage phosphorus (e.g., monomers comprising sm01, sm18, etc.). In some embodiments, X^C is O. In some embodiments, X^C is S. In some embodiments, one R^{C5} is $-H$. In some embodiments, one R^{C6} is $-H$. In some embodiments, a compound has the structure of $H-X^C-CHR^{C5}-CHR^{C6}-SH$ or a salt thereof. In some

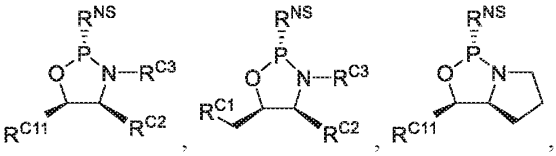
embodiments, R^{C5} is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{C5} is optionally substituted C_{1-6} alkyl. In some embodiments, R^{C5} is methyl. In some embodiments, R^{C6} is optionally substituted C_{1-6} aliphatic. In some embodiments, R^{C6} is optionally substituted C_{1-6} alkyl. In some embodiments, R^{C6} is methyl. In some embodiments, a compound is $HOCH(CH_3)CH(CH_3)SH$. In some embodiments, a compound is $HSCH(CH_3)CH(CH_3)SH$. In some embodiments, one R^{C5} is not hydrogen. In some embodiments, one R^{C6} is not hydrogen. In some embodiments, one R^{C5} and one R^{C6} are taken together with their intervening atoms to form an optionally substituted 3-20 (e.g., 3-15, 3-10, 5-10, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20) membered monocyclic, bicyclic or polycyclic ring having 0-5 heteroatoms. In some embodiments, a formed ring is monocyclic. In some embodiments, one R^{C5} and one R^{C6} are taken together with their intervening atoms to form an optionally substituted 4-8, 4-7, 5-8, 5-7, 4, 5, 6, 7, or 8-membered monocyclic ring. In some embodiments, a formed ring is a saturated cycloalkyl ring. In some embodiments, a formed ring is a cyclohexyl ring. In some embodiments, a formed ring is bicyclic. In some embodiments, a formed ring contain no heteroatom ring atoms. In some embodiments, each monocyclic ring unit is independently 3-10 membered, and/or is independently saturated, partially unsaturated or aromatic and has 0-5 heteroatoms. In some embodiments, a compound is  or a salt thereof, wherein the cyclohexyl ring is optionally substituted. In some embodiments, a compound is , or , or a salt thereof, wherein the cyclohexyl ring is optionally substituted. In some embodiments, a substituent is C_{1-6} aliphatic, e.g., $-C(CH_3)=CH_2$. For example, in some embodiments, a compound is . In some embodiments, a compound is  or a salt thereof, wherein the cyclohexyl ring is optionally substituted.

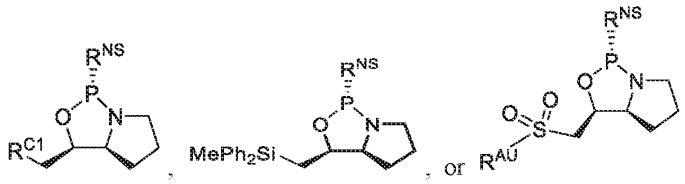
[01019] In some embodiments, methods for preparing oligonucleotides and/or compositions comprise using a chiral auxiliary described herein, e.g., for constructing one or more chirally controlled internucleotidic linkages. In some embodiments, one or more chirally controlled internucleotidic linkages are independently constructed using a DPSE chiral auxiliary. In some embodiments, each chirally controlled phosphorothioate internucleotidic linkage is independently constructed using a DPSE chiral auxiliary. In some embodiments, one or more chirally controlled internucleotidic linkages are independently constructed using



, or a salt thereof, wherein R^{AU} is as described herein. In some embodiments, each chirally controlled non-negatively charged internucleotidic linkage (e.g., n001) is independently constructed using 

, or a salt thereof. In some embodiments, each chirally controlled internucleotidic linkage is independently constructed using 

, or a salt thereof. In some embodiments, R^{AU} is optionally substituted C_{1-20}, C_{1-10}, C_{1-6}, C_{1-5}, or C_{1-4} aliphatic. In some embodiments, R^{AU} is optionally substituted C_{1-20}, C_{1-10}, C_{1-6}, C_{1-5}, or C_{1-4} alkyl. In some embodiments, R^{AU} is optionally substituted aryl. In some embodiments, R^{AU} is phenyl. In some embodiments, one or more chirally controlled internucleotidic linkages are constructed using a PSM chiral auxiliary. In some embodiments, each chirally controlled non-negatively charged internucleotidic linkage (e.g., n001) is independently constructed using a PSM chiral auxiliary. In some embodiments, each chirally controlled internucleotidic linkages is independently constructed using a PSM chiral auxiliary. As appreciated by those skilled in the art, a chiral auxiliary is often utilized in a phosphoramidite (e.g., 
or 
(DPSE phosphoramidites), 
or 
(wherein R^{AU} is independently as described herein; when R^{AU} is −Ph, PSM phosphoramidites), wherein R^{NS} is an optionally substituted/protected nucleoside (e.g., optionally protected for oligonucleotide synthesis), or a salt thereof, etc.) for oligonucleotide preparation. In some embodiments, a phosphoramidite is a compound having the structure of 
, 

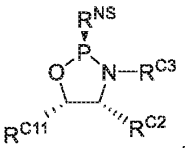
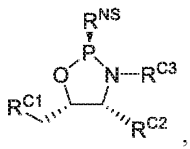
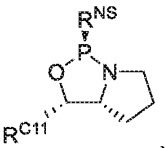
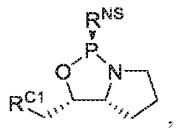
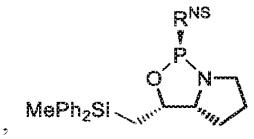
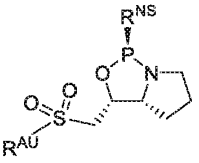


, or salt thereof, wherein each variable is independently as described herein. In some embodiments, R^{AU} is optionally substituted phenyl. In some embodiments, R^{AU} is phenyl. In some embodiments, R^{NS} is an optionally substituted or protected nucleoside comprising hypoxanthine. In some embodiments, R^{NS} comprises optionally substituted or protected hypoxanthine. In some embodiments, R^{NS} is optionally substituted or protected inosine. In some embodiments, R^{NS} is optionally substituted or protected deoxyinosine. In some embodiments, R^{NS} is optionally substituted or protected 2'-F inosine (2'-OH replaced with 2'-F). In some embodiments, R^{NS} is optionally substituted or protected 2'-OR modified inosine (2'-OH replaced with a 2'-OR modification as described herein (e.g., 2'-OMe, 2'-MOE, etc.)). In some embodiments, hypoxanthine is O^6 protected. In some embodiments, hypoxanthine is O^6 protected with $-L-Si(R)_3$, wherein L is optionally substituted $-CH_2-CH_2-$, and each R is independently as described herein and not $-H$. In some embodiments, each R is independently an optionally substituted group selected from C_{1-6} aliphatic and phenyl. In some embodiments, each R is independently optionally substituted C_{1-6} alkyl. In some embodiments, $-L-Si(R)_3$ is $-CH_2CH_2Si(Me)_3$. In some embodiments, compounds comprising O^6 protected hypoxanthine (e.g., with $-CH_2CH_2Si(Me)_3$) have higher solubility than corresponding O^6 unprotected compounds and may provide various benefits and advantages when utilized for oligonucleotide synthesis in accordance with the present disclosure. In some embodiments, in a compound having the structure of

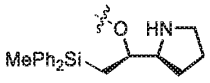
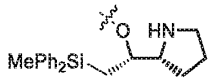
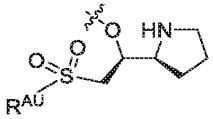
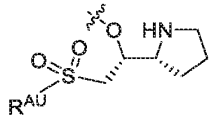
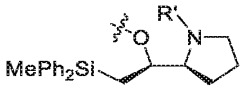
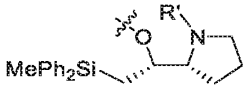
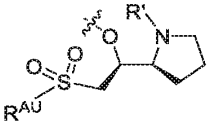
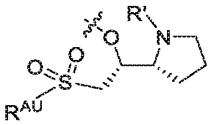
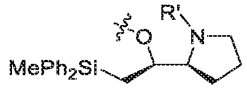
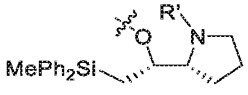
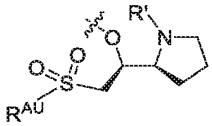
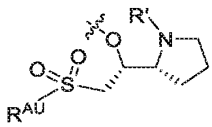


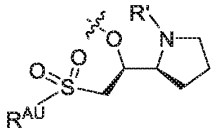
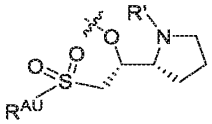
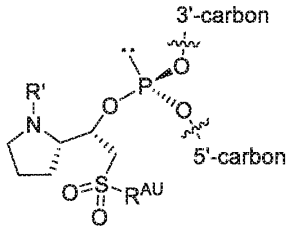
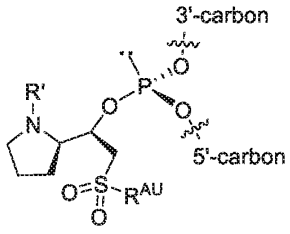
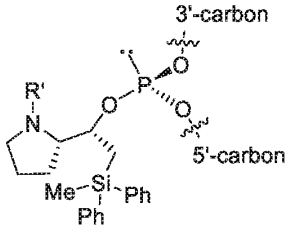
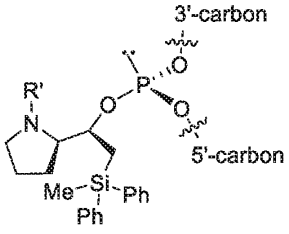


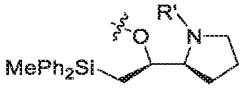
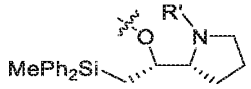
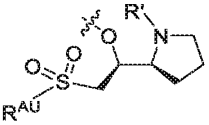
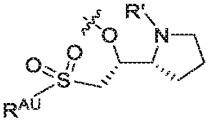
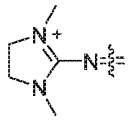
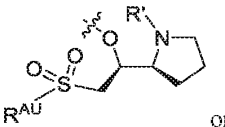
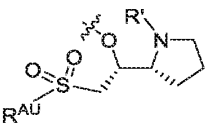
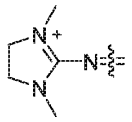
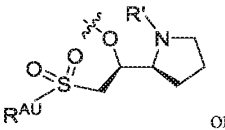
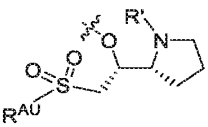
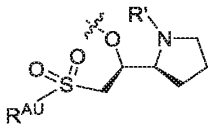
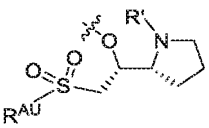
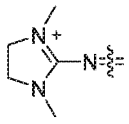
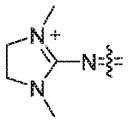
, or salt thereof, R^{NS} comprises an O^6 protected hypoxanthine (e.g., with $-CH_2CH_2Si(Me)_3$). In some embodiments, R^{NS} is O^6-protected inosine. In some embodiments, R^{NS} is O^6-protected deoxyinosine. In some embodiments, R^{NS} is O^6-protected 2'-F inosine. In some embodiments, R^{NS} is O^6-protected 2'-OR modified inosine whose 2'-OR modification is as

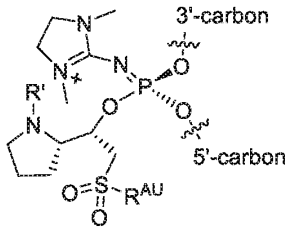
described herein (e.g., 2'-OMe, 2'-MOE, etc.). Among other things, the present disclosure encompasses the recognition that such a compound has sufficient solubility for oligonucleotide synthesis and can be utilized in oligonucleotide synthesis while a corresponding compound without O^6 protection may not have sufficient solubility for efficient oligonucleotide synthesis. In some embodiments, a phosphoramidite is (1S,3S,3aS)-1-(((2R,3S,5R)-2-((bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-5-(6-(2-(trimethylsilyl)ethoxy)-9H-purin-9-yl)tetrahydrofuran-3-yl)oxy)-3-((methyldiphenylsilyl)methyl)tetrahydro-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaphosphole. In some embodiments, a phosphoramidite is (1S,3S,3aS)-1-(((2R,3S,5R)-2-((bis(4-methoxyphenyl)(phenyl)methoxy)methyl)-5-(6-(2-(trimethylsilyl)ethoxy)-9H-purin-9-yl)tetrahydrofuran-3-yl)oxy)-3-((phenylsulfonyl)methyl)tetrahydro-1H,3H-pyrrolo[1,2-c][1,3,2]oxazaphosphole. In some embodiments, in a compound having the structure of , , , , , or , or salt thereof, R^{NS} comprises an O^6 unprotected hypoxanthine. In some embodiments, R^{NS} is optionally substituted or protected inosine wherein the hypoxanthine is unprotected. In some embodiments, R^{NS} is optionally substituted or protected deoxyinosine wherein the hypoxanthine is unprotected. In some embodiments, R^{NS} is optionally substituted or protected 2'-F inosine wherein the hypoxanthine is unprotected. In some embodiments, R^{NS} is optionally substituted or protected 2'-OR modified inosine wherein the hypoxanthine is unprotected and whose 2'-OR modification is as described herein (e.g., 2'-OMe, 2'-MOE, etc.). Among other things, the present disclosure encompasses the recognition that such a compound has sufficient solubility for oligonucleotide synthesis and can be utilized in oligonucleotide synthesis without O^6 protection.

[01020] In some embodiments, a method comprises providing a DPSE and/or a PSM phosphoramidite or a salt thereof. In some embodiments, a provided method comprises contacting a DPSE and/or a PSM phosphoramidite or a salt thereof with −OH (e.g., 5'−OH of a nucleoside or an oligonucleotide chain). As those skilled in the art appreciate, contacting can be performed under various suitable conditions so that a phosphorus linkage is formed. In some embodiments, preparation of each chirally controlled internucleotidic linkage independently comprises contacting a DPSE or PSM phosphoramidite or a salt thereof with −OH (e.g., 5'−OH of a nucleoside or an oligonucleotide chain). In some embodiments, preparation of each chirally controlled phosphorothioate internucleotidic linkage independently comprises contacting a DPSE phosphoramidite or a salt thereof with −OH (e.g., 5'−OH of a nucleoside or an oligonucleotide chain). In some embodiments, preparation of each chirally controlled non-negatively charged internucleotidic linkage (e.g.,

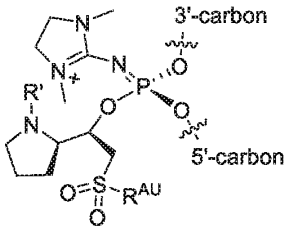
n001) independently comprises contacting a PSM phosphoramidite or a salt thereof with −OH (e.g., 5'−OH of a nucleoside or an oligonucleotide chain). In some embodiments, preparation of each chirally controlled internucleotidic linkage independently comprises contacting a PSM phosphoramidite or a salt thereof with −OH (e.g., 5'−OH of a nucleoside or an oligonucleotide chain). In some embodiments, contacting forms a P(III) linkage comprising a phosphorus atom bonded to two sugars and a chiral auxiliary moiety (e.g.,  or , or a salt form thereof (e.g., from DPSE phosphoramidites or salts thereof),  or , or a salt form thereof (wherein R^{AU} is independently as described herein; when R^{AU} is −Ph, e.g., from PSM phosphoramidites or salts thereof), etc.). In some embodiments, an oligonucleotide comprises a P(III) linkage comprising a chiral auxiliary moiety, e.g., from a DPSE or PSM phosphoramidite. In some embodiments, a P(III) linkage comprising a chiral auxiliary moiety is chirally controlled. In some embodiments, a chiral auxiliary moiety may be protected, e.g., before converting a P(III) linkage to a P(V) linkage (e.g., before sulfurization, reacting with azide, etc.). In some embodiments, a protected chiral auxiliary has the structure of  or , or a salt form thereof (e.g., wherein R' is independently as described herein; e.g., from DPSE phosphoramidites or salts thereof), or  or , or a salt form thereof (wherein each R' and R^{AU} is independently as described herein; when R^{AU} is −Ph, e.g., from PSM phosphoramidites or salts thereof), wherein each R' is independently as described herein. In some embodiments, R' is −C(O)R, wherein R is as described herein. In some embodiments, R is $-CH_3$. In some embodiments, an oligonucleotide comprises a protected chiral auxiliary. In some embodiments, each chirally controlled internucleotidic linkage in an oligonucleotide independently comprises  or , or a salt form thereof, or  or , or a salt form thereof. In some embodiments, each chirally controlled internucleotidic linkage in an oligonucleotide

independently comprises  or , or a salt form thereof. In some embodiments, R' is −C(O)R. In some embodiments, R' is −C(O)CH_3. In some embodiments, R^{AU} is Ph. In some embodiments, an oligonucleotide comprises one or more  or a salt form thereof (PIII-1), wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or more  or a salt form thereof (PIII-2), wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or more  or a salt form thereof (PIII-5), wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or more  or a salt form thereof (PIII-6), wherein each variable independently as described herein. In some embodiments, a 5'-end internucleotidic linkage is PIII-1, PIII-2, PIII-5, or PIII-6. In some embodiments, a 5'-end internucleotidic linkage is PIII-1 or PIII-2. In some embodiments, R' is −H. In some embodiments, R' is −C(O)R. In some embodiments, R' is −C(O)CH_3. In some embodiments, R^{AU} is −Ph. In some embodiments, a P(III) linkage is converted into a P(V) linkage. In some embodiments, a P(V) linkage

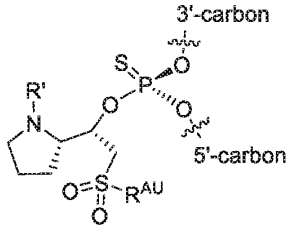
comprises a phosphorus atom bonded to two sugars, a chiral auxiliary moiety (e.g., 
or , or a salt form thereof (wherein R' is as described herein; e.g., from DPSE phosphoramidites or salts thereof),  or , or a salt form thereof (wherein each of R' and R^{AU} is independently as described herein; when R^{AU} is –Ph, e.g., from PSM phosphoramidites or salts thereof), etc.), and S or . In some embodiments, a P(V) linkage comprises a phosphorus atom bonded to two sugars,  or , or a salt form thereof (wherein each R' and R^{AU} is independently as described herein; when R^{AU} is –Ph, e.g., from PSM phosphoramidites or salts thereof), etc.), and S or . In some embodiments, a P(V) linkage comprises a phosphorus atom bonded to two sugars,  or , or a salt form thereof (wherein each R' and R^{AU} is independently as described herein; when R^{AU} is –Ph, e.g., from PSM phosphoramidites or salts thereof), etc.), and S. In some embodiments, a P(V) linkage comprises a phosphorus atom bonded to two sugars,  or , or a salt form thereof (wherein each R' and R^{AU} is independently as described herein; when R^{AU} is –Ph, e.g., from PSM phosphoramidites or salts thereof), etc.), and . Those skilled in the art will appreciate that  can exist with a counterion, e.g., in some embodiments, PF_6^-. In some embodiments, an oligonucleotide comprises one or



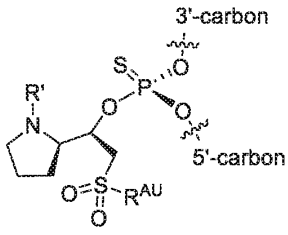
more or a salt form thereof (PV-1) , wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or more



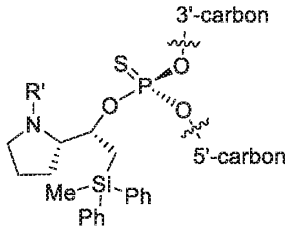
or a salt form thereof (PV-2) , wherein each variable independently as described



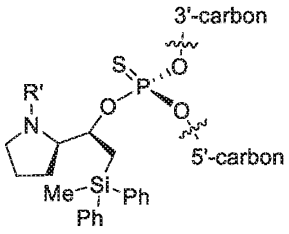
herein. In some embodiments, an oligonucleotide comprises one or more or a salt form thereof (PV-3) , wherein each variable independently as described herein. In some embodiments, an

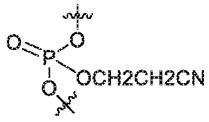


oligonucleotide comprises one or more or a salt form thereof (PV-4) , wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or



more or a salt form thereof (PV-5) , wherein each variable independently as described herein. In some embodiments, an oligonucleotide comprises one or more

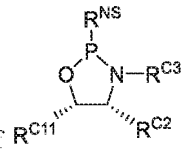
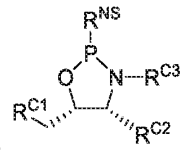
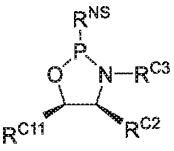
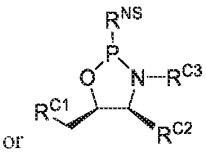
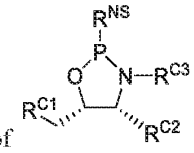
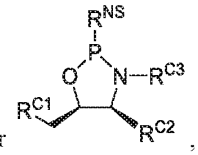
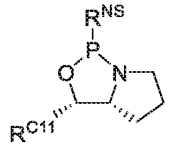


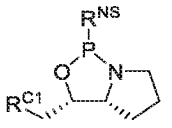
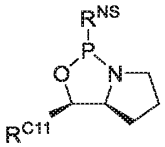
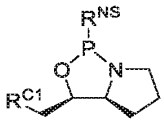
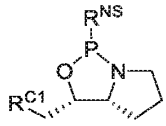
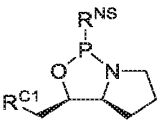
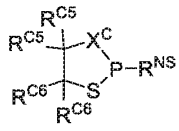
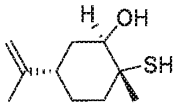
or a salt form thereof (PV-6) , wherein each variable independently as described herein. In some embodiments, each chiral internucleotidic linkage, or each chirally controlled internucleotidic linkage, of an oligonucleotide is independently selected from PIII-1, PIII-2, PIII-5, PIII-6, PV-1, PV-2, PV-3, PV-4, PV-5, and PV-6. In some embodiments, each chiral internucleotidic linkage, or each chirally controlled internucleotidic linkage, of an oligonucleotide is independently selected from PIII-1, PIII-2, PV-1, PV-2, PV-3, and PV-4. In some embodiments, a linkage of PIII-1, PIII-2, PIII-5, or PIII-6 is typically the 5'-end internucleotidic linkage. In some embodiments, each chiral internucleotidic linkage, or each chirally controlled internucleotidic linkage, of an oligonucleotide is independently selected from PV-1, PV-2, PV-3, PV-4, PV-5, and PV-6. In some embodiments, each chiral internucleotidic linkage, or each chirally controlled internucleotidic linkage, of an oligonucleotide is independently selected from PV-1, PV-2, PV-3, or PV-4. In some embodiments, a provided oligonucleotide is an oligonucleotide as described herein, e.g., of Table 1 or Table 1A, wherein each *S is independently replaced with PV-3 or PV-5, each *R is independently replaced with PV-4 or PV-6, each n001R is independently replaced with PV-1, and each n001S is independently replaced with PV-2. In some embodiments, a provided oligonucleotide is an oligonucleotide as described herein, e.g., of Table 1 or Table 1A, wherein each *S is independently replaced with PV-3, each *R is independently replaced with PV-4, each n001R is independently replaced with PV-1, and each n001S is independently replaced with PV-2. In some embodiments, each natural phosphate linkage is independently replaced with a precursor, e.g., 

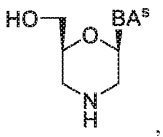
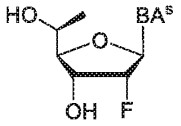
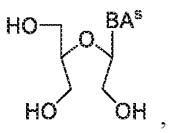
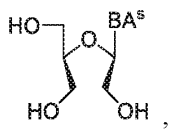
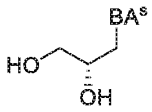
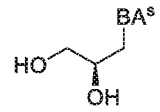
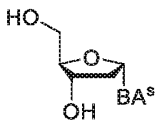
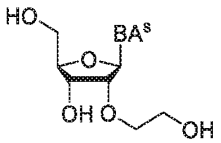
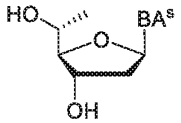
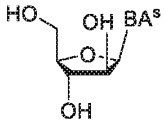
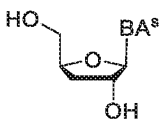
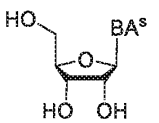
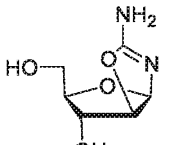
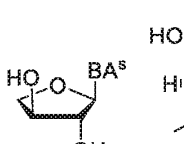
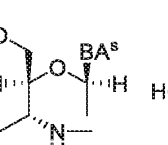
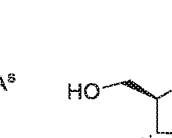
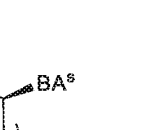
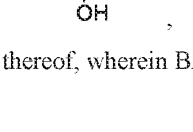
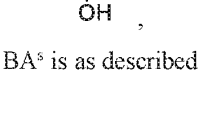
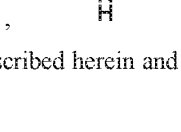
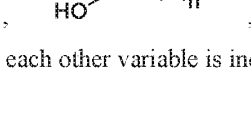
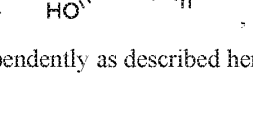
. In some embodiments, R' is −H. In some embodiments, R' is −C(O)R. In some embodiments, R' is $-C(O)CH_3$. In some embodiments, R^{AU} is −Ph. In some embodiments, a method comprises removal of one or more chiral auxiliary moieties so that phosphorothioate and/or non-negatively charged internucleotidic linkages (e.g., n001) are formed (e.g., from V-1, PV-2, PV-3, PV-4, PV-5, PV-6, etc.). In some embodiments, removal of a chiral auxiliary (e.g., PSM) comprises contacting an oligonucleotide with a base (e.g., $N(R)_3$ such as DEA) under anhydrous conditions.

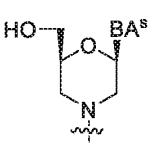
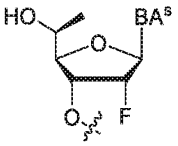
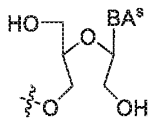
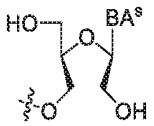
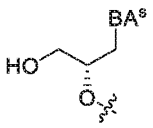
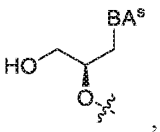
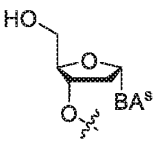
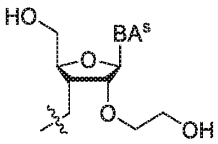
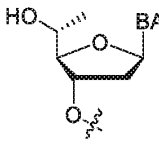
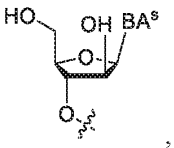
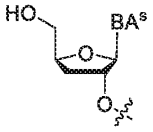
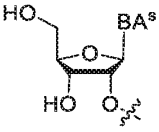
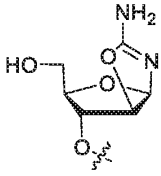
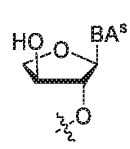
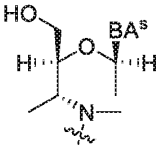
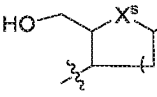
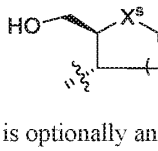
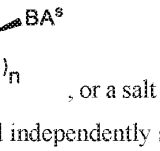
[01021] In some embodiments, as appreciated by those skilled in the art, for preparation of a chirally controlled internucleotidic linkage, a monomer or a phosphoramidite (e.g., a DPSE or PSM phosphoramidite) is typically utilized in a chirally enriched or pure form (e.g., of a purity as described herein (e.g., about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, or about 100%)).

[01022] In some embodiments, the present disclosure provides useful reagents for preparation of

oligonucleotides and compositions thereof. In some embodiments, monomers and phosphoramidites comprise nucleosides, nucleobases and sugars as described herein. In some embodiments, nucleobases and sugars are properly protected for oligonucleotide synthesis as those skilled in the art will appreciate. In some embodiments, a phosphoramidite has the structure of R^{NS}–P(OR)N$(R)_2$, wherein R^{NS} is a optionally protected nucleoside moiety. In some embodiments, a phosphoramidite has the structure of R^{NS}–P(OCH_2CH_2CN)N(i-Pr)$_2$. In some embodiments, a monomer comprises a nucleobase which is or comprises Ring BA, wherein Ring BA has the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA, wherein the nucleobase is optionally substituted or protected. In some embodiments, a phosphoramidite comprises a nucleobase which is or comprises Ring BA, wherein Ring BA has the structure of BA-I, BA-I-a, BA-I-b, BA-I-c, BA-I-d, BA-II, BA-II-a, BA-II-b, BA-II-c, BA-II-d, BA-III, BA-III-a, BA-III-b, BA-III-c, BA-III-d, BA-III-e, BA-IV, BA-IV-a, BA-IV-b, BA-V, BA-V-a, BA-V-b, or BA-VI, or a tautomer of Ring BA, wherein the nucleobase is optionally substituted or protected. In some embodiments, a phosphoramidite comprises a chiral auxiliary moiety, wherein the phosphorus is bonded to an oxygen and a nitrogen atom of the chiral auxiliary moiety. In some embodiments, a phosphoramidite has the structure of , , , or , or a salt thereof, wherein R^{NS} is a protected nucleoside moiety (e.g., 5'-OH and/or nucleobases suitably protected for oligonucleotide synthesis), and each other variable is independently as described herein. In some embodiments, a phosphoramidite has the structure of  or , wherein R^{NS} is a protected nucleoside moiety (e.g., 5'-OH and/or nucleobases suitably protected for oligonucleotide synthesis), R^{C1} is R, $-Si(R)_3$ or $-SO_2R$, and R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 3-7 membered saturated ring having, in addition to the nitrogen atom, 0-2 heteroatoms, wherein the coupling forms an internucleotidic linkage. In some embodiments, 5'-OH of R^{NS} is protected. In some embodiments, 5'-OH of R^{NS} is protected as $-$ODMTr. In some embodiments, R^{NS} is bonded to phosphorus through its 3'-O-. In some embodiments, a formed ring by R^{C2} and R^{C3} is an optionally substituted 5-membered ring. In some embodiments, a phosphoramidite has the structure of ,



or , or a salt thereof. In some embodiments, a phosphoramidite has the structure of  or . In some embodiments, as described herein R^{NS} comprises a modified nucleobase (e.g., b001A, b002A, b003A, b008U, b001C, etc.) which is optionally protected for oligonucleotide synthesis. In some embodiments, a monomer has the structure of  or a salt thereof, wherein R^{NS} is an optionally substituted/protected nucleoside (e.g., optionally protected for oligonucleotide synthesis) as described herein, and each other variable is independently as described herein. In some embodiments, $-X^C-C(R^{C5})_2-C(R^{C6})_2-S-$ is of such a structure that $H-X^C-C(R^{C5})_2-C(R^{C6})_2-SH$ is a compound as described herein, e.g., $HOCH(CH_3)CH(CH_3)SH$, $HSCH(CH_3)CH(CH_3)SH$, , etc. In some embodiments, 5'-OH of R^{NS} is protected. In some embodiments, 5'-OH of R^{NS} is protected as −ODMTr.

In some embodiments, R^{NS} is an optionally substituted or protected nucleoside selected from , , , , , , , , , , , , , , , , , , , , , or , or a salt thereof, wherein BA^s is as described herein and each other variable is independently as described herein.. In

some embodiments, R^{NS} is  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  , , , , , or , or a salt thereof, wherein BA^s is as described herein. In some embodiments, each −OH is optionally and independently substituted or protected. In some embodiments, BA^s is optionally substituted or protected nucleobase, and each −OH of the nucleoside is independently protected, wherein at least one −OH is protected as DMTrO−. In some embodiments, −OH for coupling, e.g., with another monomer or phosphoramidite, is protected as DMTrO−. In some embodiments, an −OH group for coupling, e.g., with another monomer or phosphoramidite, is protected different from an −OH group that is not for coupling. In some embodiments, a non-coupling −OH is protected such that the protection remains when DMTrO− is deprotected. In some embodiments, a non-coupling −OH is protected such that the protection remains during oligonucleotide synthesis cycles. In some embodiments, BA^s is an optionally protected nucleobase selected from A, T, C, G, U, and tautomers thereof. In some embodiments, BA^s is an optionally protected nucleobase selected from Table BA-1 and tautomers thereof. In some embodiments, BA^s is an optionally protected nucleobase selected for b004A, b005A, b006A, b007A, b014U, and b015U, and tautomers thereof. In some embodiments, X^s is −O−. In some embodiments, X^s is −S−. In some embodiments, X^s is −Se−. In some embodiments, X^s is optionally substituted $-CH_2-$. In some embodiments, X^s is $-CH_2-$. In some embodiments, n is 0. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, R^{NS} comprises an optionally substituted or protected nucleobase as described herein (e.g., selected from Table BA-1) or a tautomer thereof and a sugar as described herein.

[01023] In some embodiments, purity or stereochemical purity of a monomer or a phosphoramidite is at least 85%, 90%, 95%, 96%, 97%, 98%, or 99%. In some embodiments, it is at least 85%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%.

[01024] In some embodiments, the present disclosure provides a method for preparing an oligonucleotide or composition, comprising coupling a free −OH, e.g., a free 5'-OH, of an oligonucleotide or a nucleoside with

a monomer as described herein. In some embodiments, the present disclosure provides a method for preparing an oligonucleotide or composition, comprising coupling a free −OH, e.g., a free 5'-OH, of an oligonucleotide or a nucleoside with a phosphoramidite as described herein.

[01025] In some embodiments, the present disclosure provides an oligonucleotide, wherein the oligonucleotide comprises one or more modified internucleotidic linkages each independently having the structure of $-O^5-P^L(W)(R^{CA})-O^3-$, wherein:

P^L is P, or P(=W);

W is O, S, or W^N;

W^N is $=N-C(-N(R^1)_2=N^+(R^1)_2Q^-$;

Q^- is an anion;

R^{CA} is or comprises an optionally capped chiral auxiliary moiety,

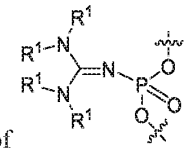
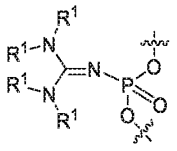
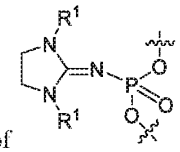
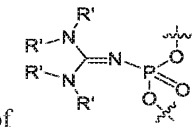
O^5 is an oxygen bonded to a 5'-carbon of a sugar, and

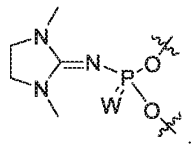
O^3 is an oxygen bonded to a 3'-carbon of a sugar.

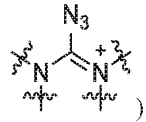
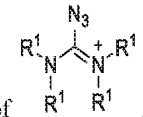
[01026] In some embodiments, a modified internucleotidic linkage is optionally chirally controlled. In some embodiments, a modified internucleotidic linkage is optionally chirally controlled.

[01027] In some embodiments, a provided methods comprising removing R^{CA} from such a modified internucleotidic linkages. In some embodiments, after removal, bonding to R^{CA} is replaced with −OH. In some embodiments, after removal, bonding to R^{CA} is replaced with =O, and bonding to W^N is replaced with $-N=C(N(R^1)_2)_2$.

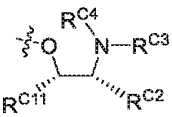
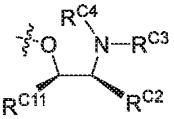
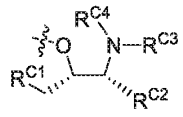
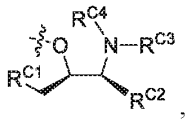
[01028] In some embodiments, P^L is P=S, and when R^{CA} is removed, such an internucleotidic linkage is converted into a phosphorothioate internucleotidic linkage.

[01029] In some embodiments, P^L is $P=W^N$, and when R^{CA} is removed, such an internucleotidic linkage is converted into an internucleotidic linkage having the structure of . In some embodiments, an internucleotidic linkage having the structure of  has the structure of . In some embodiments, an internucleotidic linkage having the structure of  has the structure of



[01030] In some embodiments, P^L is P (e.g., in newly formed internucleotidic linkage from coupling of a phosphoramidite with a 5'-OH). In some embodiments, W is O or S. In some embodiments, W is S (e.g., after sulfurization). In some embodiments, W is O (e.g., after oxidation). In some embodiments, certain non-negatively charged internucleotidic linkages or neutral internucleotidic linkages may be prepared by reacting a P(III) phosphite triester internucleotidic linkage with azido imidazolinium salts (*e.g.*, compounds comprising ) under suitable conditions. In some embodiments, an azido imidazolinium salt is a salt of PF_6^-. In some embodiments, an azido imidazolinium salt is a salt of  . In some embodiments, an azido imidazolinium salt is 2-azido-1,3-dimethylimidazolinium hexafluorophosphate.

[01031] As appreciated by those skilled in the art, Q^- can be various suitable anion present in a system (e.g., in oligonucleotide synthesis), and may vary during oligonucleotide preparation processes depending on cycles, process stages, reagents, solvents, etc. In some embodiments, Q^- is OH^-. In some embodiments, W^N is $=N-C(-N(R^1)_2=N(R^1)_2OH$. In some embodiments, W^N is a salt form of $=N-C(-N(R^1)_2=N(R^1)_2OH$. In some embodiments, Q^- is PF_6^-.

[01032] In some embodiments, R^{CA} is  or  , wherein R^{C4} is $-H$ or $-C(O)R'$, and each other variable is independently as described herein. In some embodiments, R^{CA} is  or  , wherein R^{C1} is R, $-Si(R)_3$ or $-SO_2R$, R^{C2} and R^{C3} are taken together with their intervening atoms to form an optionally substituted 3-7 membered saturated ring having, in addition to the nitrogen atom, 0-2 heteroatoms, R^{C4} is $-H$ or $-C(O)R'$. In some embodiments, R^{C4} is $-H$. In some embodiments, R^{C4} is $-C(O)CH_3$. In some embodiments, R^{C2} and R^{C3} are taken together to form an optionally substituted 5-membered ring.

[01033] In some embodiments, R^{C4} is $-H$ (e.g., in n newly formed internucleotidic linkage from coupling of a phosphoramidite with a 5'-OH). In some embodiments, R^{C4} is $-C(O)R$ (e.g., after capping of the amine). In some embodiments, R is methyl.

[01034] In some embodiments, each chirally controlled phosphorothioate internucleotidic linkage is independently converted from $-O^5-P^L(W)(R^{CA})-O^3-$.

Assessment/Characterization of Providing Technologies

[01035] As appreciated by those skilled in the art, various technologies may be utilized to assess/characterize provided technologies in accordance with the present disclosure. Certain useful technologies are described in the Examples; as demonstrated, among other things, the present disclosure describes various *in vivo* and *in vitro* technologies suitable for assessing and characterizing provided technologies. In some embodiments, provided technologies are assessed/characterized, e.g., in cells, with or without exogenous ADAR polypeptides; additionally or alternatively, in some embodiments, provided technologies are assessed/characterized, e.g., in animals, e.g., non-human primates and mice.

[01036] Among other things, the present disclosure encompasses the insights that various agents (e.g., oligonucleotides) and compositions thereof that can provide editing in various human systems, e.g., cells, may show no or much lower levels of editing in certain cells (e.g., mouse cells) and certain animals such as rodents (e.g., mice) that do not contain or express human ADAR, e.g., human ADAR1. Particularly, mice, a commonly used animal model, may be of limited uses for assessing various agents (e.g., oligonucleotides) for editing in humans, as various agents active in human cells provide no or very low levels of activity in mouse cells and animals not engineered to comprise or express a proper ADAR1 (e.g., human ADAR1) polypeptide or a characteristic portion thereof. In some embodiments, the present disclosure provides engineered cells and non-human animals expressing human ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, such cells and human are useful for assessing and characterizing provided technologies. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises human ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises human ADAR1 p110 polypeptide or a characteristic portion thereof. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises human ADAR1 p150 polypeptide or a characteristic portion thereof. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises human ADAR1. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises a human ADAR1 p110 peptide. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises a human ADAR1 p150 peptide. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises one or more or all of the following domains of human ADAR1: Z-DNA binding domains, dsRNA binding domains, and deaminase domain. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises one or both of human ADAR1 Z-DNA binding domains; alternatively or additionally, in some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises one, two or all of human ADAR1 dsRNA binding domains; alternatively or additionally, a human ADAR1 polypeptide or a characteristic portion thereof is or comprises a human deaminase domain. In some embodiments, a human ADAR1 polypeptide or a characteristic portion thereof

may be expressed together with a mouse ADAR1 polypeptide or a characteristic portion thereof, e.g., one or more human dsRNA binding domains may be engineered to be expressed together with a mouse deaminase domain to form a human-mouse hybrid ADAR1 polypeptide. In some embodiments, cells and/or non-human animals are engineered to comprise and/or express a polynucleotide encoding a human ADAR1 polypeptide or a characteristic portion thereof as described herein. In some embodiments, genomes of cells and/or non-human animals are engineered to comprise a polynucleotide encoding a human ADAR1 polypeptide or a characteristic portion thereof as described herein. In some embodiments, germline genomes of cells and/or non-human animals are engineered to comprise a polynucleotide encoding a human ADAR1 polypeptide or a characteristic portion thereof as described herein. In some embodiments, cells and non-human animals are engineered to comprise, e.g., in their genomes (in some embodiments, germline genomes), one or more mutations (e.g., a mutation within the same amino acid codon as an adenosine) each independently associated with a condition, disorder or disease. As demonstrated herein, among other things such cells and animals are useful for assessing/characterizing provided technologies, e.g., various oligonucleotides and compositions thereof, e.g., for their editing properties and/or activities, including for their uses against one or more conditions, disorders or diseases. In some embodiments, cells are rodent cells. In some embodiments, cells are mouse cells. In some embodiments, an animal is a rodent. In some embodiments, an animal is a mouse.

[01037] Among other things, the present disclosure provides oligonucleotide designs comprising sugar modifications, base modifications, internucleotidic linkage modifications, linkage phosphorus stereochemistry, and/or patterns thereof, that can greatly improve one or more properties and/or activities of oligonucleotides compared to comparable oligonucleotides of similar or identical base sequences but of reference designs. For example, it was observed that oligonucleotides of various provided designs and compositions thereof can provide high levels of editing in mice that do not express a human ADAR protein (e.g., mice only expressing mouse ADAR proteins), in some embodiments comparable to or no lower than in mice that are engineered to express a human ADAR protein, while comparable oligonucleotides of reference designs and compositions thereof provide low levels of editing in mice that do not express a human ADAR protein (e.g., mice only expressing mouse ADAR proteins), in some embodiments significantly lower than in mice that are engineered to express a human ADAR protein. In some embodiments, a reference design is a design reported in WO 2016/097212, WO 2017/220751, WO 2018/041973, WO 2018/134301A1, WO 2019/158475, WO 2019/219581, WO 2020/157008, WO 2020/165077, WO 2020/201406, WO 2020/252376, WO 2021/130313, WO 2022/018207, or WO 2023/152371. In some embodiments, a reference design is a design in WO 2021/071858. In some embodiments, a reference design is a design in WO 2022/099159.

[01038] In some embodiments, the present disclosure provides technologies for assessing/characterizing for assessing cells and/or non-human animals, including those engineered to comprise or express an ADAR1 polypeptide or a characteristic portion thereof, or a polynucleotide encoding an ADAR1 polypeptide or a characteristic portion thereof, which ADAR1 polypeptide or a characteristic portion thereof and/or polynucleotide is not in and/or is not expressed in the cells and/or non-human animals prior to engineering. In

some embodiments, a provided method comprises administering to a cell or a population thereof one or more oligonucleotides or compositions which one or more oligonucleotides or compositions can each independently edit an adenosine in a comparable human cell or a population thereof. In some embodiments, a provided method comprises administering to an animal or a population thereof one or more oligonucleotides or compositions which one or more oligonucleotides or compositions can each independently edit an adenosine in a human cell or a population thereof. In some embodiments, editing levels in cells to be assessed/characterized, or in cells from animals, are compared to those observed in comparable human cells. In some embodiments, comparable human cells are of the same type as cells to be assessed/characterized or cells from animals. In some embodiments, cells are rodent cells. In some embodiments, cells are mouse cells. In some embodiments, an animal is a rodent. In some embodiments, an animal is a mice. In some embodiments, one or more oligonucleotides or compositions are administered separately to separate cells and/or animals. In some embodiments, one or more oligonucleotides or compositions may be administered to the same collection of cells and/or animals, optionally simultaneously. Various oligonucleotides and compositions that can edit various target adenosines are as described herein and can be utilized accordingly.

[01039] As appreciated by those skilled in the art, in some embodiments, provided technologies, e.g., oligonucleotides, compositions, etc., may be assessed in one or more models, e.g., cells, tissues, organs, animals, etc. In some embodiments, as appreciated by those skilled in the art, cells, tissues, organs, animals, etc. are or comprise cells of, associated with or comprising one or more characteristics (e.g., nucleotide sequences such as mutations) of conditions, disorders or diseases. In some embodiments, cells, tissues, organs, animals, etc. comprise one or more cancer cells. In some embodiments, non-human cells, tissues, organs, animals, etc. are engineered to comprise or express ADAR1 or a characteristic portion thereof, e.g., through incorporation of (optionally into its genome or germline genome) a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, an ADAR1 is a primate ADAR1. In some embodiments, an ADAR1 is a human ADAR1. In some embodiments, a human ADAR1 is human ADAR1 p110. In some embodiments, a human ADAR1 is human ADAR1 p150. As appreciated by those skilled in the art, various technologies are available in the art and can be utilized in accordance with the present disclosure to generated useful cells, tissues, organs, animals, etc. For example, for condition, disorder or disease animal models expressing human ADAR1 or a characteristic portion thereof, an animal model can be crossed with huADAR1 mice described herein to provide engineered animal models expressing human ADAR1 or a characteristic portion thereof. In some embodiments, mice comprising certain mutations (e.g., PNPLA3 I148M mutation) are crossed with huADAR1 mice described herein to provide mice comprising such mutations and expressing human ADAR1 or a characteristic portion thereof. Certain useful technologies including useful transgenic mice are described in WO 2021/071858, WO 2022/046667, or WO 2022/099159.

[01040] As appreciated by those skilled in the art, in some embodiments, animals can be heterozygous with respect to one or more or all sequences. In some embodiments, animals are homozygous with respect to one or more or all sequences. In some embodiments, animals are hemizygous with respect to one or more or all

engineered sequences. In some embodiments, animals are homozygous with respect to one or more sequences, and heterozygous with respect to one or more sequences. In some embodiments, animals are heterozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, animals are homozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, certain animals are heterozygous with respect to one or more polynucleotide sequences associated with various condition, disorder or diseases, and are heterozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, certain animals are homozygous with respect to one or more polynucleotide sequences associated with various condition, disorder or diseases, and are heterozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, certain animals are heterozygous with respect to one or more polynucleotide sequences associated with various condition, disorder or diseases, and are homozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, certain animals are homozygous with respect to one or more polynucleotide sequences associated with various condition, disorder or diseases, and are homozygous with respect to a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. Cells or tissues may be similarly heterozygous, hemizygous and/or homozygous with respect to various sequences.

[01041] In some embodiments, the present disclosure provides methods for assessing an agent, e.g., an oligonucleotide, or a composition thereof, comprising administering to an animal, cell or tissue described herein the agent or composition. In some embodiments, an agent or composition is assessed for preventing or treating a condition, disorder or disease. In some embodiments, animals, cells, tissues, e.g., as described in various embodiments herein, are animal models, or cells or tissues, for various conditions, disorders or diseases (e.g., comprising mutations associated with various conditions, disorders or diseases, and/or cells, tissues, organs, etc., associated with or of various conditions, disorders or diseases) that are engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, animals may be provided by breeding (e.g., IVF, natural breeding, etc.) an animal that are model animals for various conditions, disorders or diseases but are not engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof with animals that are engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, cells or tissues may be provided by introducing into cells or tissues a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising administering to a subject an effective amount of an agent or a compositions thereof, wherein the agent or composition is assessed in an animal provided herein (e.g., an animal engineered to comprise an ADAR1 polypeptide or a characteristic portion thereof, an animal engineered to comprise and/or express a polynucleotide whose sequence encodes an

ADAR1 polypeptide or a characteristic portion thereof, a model animal for a condition, disorder or disease which is engineered to comprise an ADAR1 polypeptide or a characteristic portion thereof, a model animal for a condition, disorder or disease engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof). In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising administering to a subject an effective amount of an agent or a compositions thereof, wherein the agent or composition is assessed in a cell or tissue provided herein. In some embodiments, an animal is a non-human animal. In some embodiments, cells are non-human animal cells. In some embodiments, tissues are non-human animal tissues. In some embodiments, a non-human animal is a rodent. In some embodiments, a non-human animal is a mouse. In some embodiments, a non-human animal is a rat. In some embodiments, a non-human animal is a non-human primate.

[01042] In some embodiments, the present disclosure provides methods comprising: 1) assessing an agent or a composition thereof, comprising contacting the agent or a composition thereof with a provided cell or tissue associated with or of a condition, disorder or disease, and 2) administering to a subject suffering from or susceptible to a condition, disorder or disease an effective amount of an agent or composition thereof. In some embodiments, the present disclosure provides methods comprising: 1) assessing an agent or a composition thereof, comprising administering the agent or a composition thereof to a provided animal which is an animal model of a condition, disorder or disease, and 2) administering to a subject suffering from or susceptible to a condition, disorder or disease an effective amount of an agent or composition thereof. In some embodiments, as described herein, a cell, tissue or animal is engineered to comprise an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, a cell, tissue or animal is engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, a cell, tissue or animal further comprises a nucleotide sequence (e.g., a mutation) associated with a condition, disorder or disease. In some embodiments, an animal is a rodent, e.g., a mouse, a rat, etc. In some embodiments, a cell or tissue is of a rodent, e.g., a mouse, a rat, etc. In some embodiments, a cell is a germline cell. In some embodiments, a fraction of and not all cells, e.g., cells of particular cell types or tissues or location, of a population of cells, a tissue or an animal comprise a nucleotide sequence (e.g., a mutation) associated with a condition, disorder or disease, and such fraction of cells are engineered to comprise an ADAR1 polypeptide or a characteristic portion thereof or engineered to comprise and/or express a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof. Those skilled in the art appreciate that various technologies are available for optionally controlled introduction and/or expression of a nucleotide sequence in various cells, tissues, or organs and can be utilized in accordance with the present disclosure. In some embodiments, as described herein, a cell, tissue or animal comprises a polynucleotide whose sequence encodes an ADAR1 polypeptide or a characteristic portion thereof in a genome, in some embodiments, in a germline genome. In some embodiments, as described herein, a cell, tissue or animal comprises a nucleotide sequence (e.g., a mutation) associated with a condition, disorder or

disease in a genome, in some embodiments, in a germline genome.

[01043] As described herein, in some embodiments, a polynucleotide encodes human ADAR1 p110 or a characteristic portion thereof. In some embodiments, a polynucleotide encodes human ADAR1 p110. In some embodiments, a polynucleotide encodes human ADAR1 p150 or a characteristic portion thereof. In some embodiments, a polynucleotide encodes human ADAR1 p150. In some embodiments, a cell, tissue or animal (e.g., a huADAR mouse or a cell or tissue therefrom) is engineered to comprise and/or express a polynucleotide whose sequence encodes a human ADAR1 p110 polypeptide or a characteristic portion thereof. In some embodiments, a cell, tissue or animal (e.g., a huADAR mouse or a cell or tissue therefrom) is engineered to comprise and/or express a polynucleotide whose sequence encodes a human ADAR1 p110 polypeptide. In some embodiments, a cell, tissue or animal (e.g., a huADAR mouse or a cell or tissue therefrom) is engineered to comprise and/or express a polynucleotide whose sequence encodes a human ADAR1 p150 polypeptide or a characteristic portion thereof. In some embodiments, a cell, tissue or animal (e.g., a huADAR mouse or a cell or tissue therefrom) is engineered to comprise and/or express a polynucleotide whose sequence encodes a human ADAR1 p150 polypeptide. As described herein, in some embodiments, an animal is a rodent, e.g., a mouse or a rat.

[01044] Among other things, the present disclosure provides the insight that conversion of I148M in PNPLA3 into I148V (e.g., through DNA editing, RNA editing, etc.) can provide various benefits and advantages, e.g., compared to absence of conversion and/or knockdown and/or knockout of I148M mutant PNPLA3. In some embodiments, the present disclosure encompasses the recognition that certain animals, e.g., Nycticebus coucang, has functional PNPLA3 counterpart which has V at a position corresponding to I148 in human PNPLA3. In some embodiments, assessment is performed in a system comprising I148M PNPLA3 mutation. In some embodiments, a system is homozygous for I148M PNPLA3 mutation. In some embodiments, a system is or comprises primary human hepatocytes from patient donor which hepatocytes are homozygous for I148M PNPLA3 mutation. In some embodiments, a system is heterozygous for I148M PNPLA3 mutation. In some embodiments, a system comprises or expresses wide-type PNPLA3 and mutant I148M PNPLA3. In some embodiments, a system is or comprises primary human hepatocytes from patient donor which hepatocytes are heterozygous for I148M PNPLA3 mutation. In some embodiments, a system is or comprises primary human hepatocytes from patient donor which hepatocytes are heterozygous and have wide-type PNPLA3 and I148M mutant PNPLA3.

Uses and Applications

[01045] As appreciated by those skilled in the art, oligonucleotides are useful for multiple purposes. In some embodiments, provided technologies (e.g., oligonucleotides, compositions, methods, etc.) can be useful for modulating levels and/or activities of various nucleic acids (e.g., RNA) and/or products encoded thereby (e.g., proteins). In some embodiments, provided technologies can reduce levels and/or activities of undesired target nucleic acids (e.g., comprising undesired adenosine) and/or products thereof. In some embodiments, provided technologies can increase levels and/or activities of desired target nucleic acids (e.g., comprising I

instead of undesired adenosine at one or more locations) and/or products thereof. In some embodiments, provided technologies can increase levels and/or activities of desired a target PNPLA3 transcript.

[01046] For example, in some embodiments, provided technologies can be utilized as single-stranded oligonucleotides for site-directed editing of target adenosine in target RNA sequences (e.g., target PNPLA3 RNA sequences). In some embodiments, provided technologies are capable of modulating levels of expressions and activities. Among other things, the present disclosure provides improvement by provided technologies which can be improvement of various desired biological functions, including but not limited to treatment and/or prevention of various conditions, disorders or diseases.

[01047] In some embodiments, provided technologies can modulate activities and/or functions of a target gene (e.g., PNPLA3). In some embodiments, a target gene (e.g., PNPLA3) is a gene with respect to which expression and/or activity of one or more gene products (e.g., RNA and/or protein products) are intended to be altered. In many embodiments, target genes (e.g., PNPLA3) have target adenosine residues to be altered and can benefit from conversion of such residues to inosine residues. In some embodiments, when an oligonucleotide as described herein acts on a particular target gene (e.g., PNPLA3), level and/or activity of one or more gene products of that gene can be altered when the oligonucleotide is present as compared with when it is absent.

[01048] In some embodiments, provided oligonucleotides and compositions are useful for treating various conditions, disorders, or diseases, by reducing levels and/or activities of target transcripts and/or products encoded thereby that are associated with the conditions, disorders, or diseases, and optionally providing transcripts and/or products encoded thereby that are less associated or not associated with the conditions, disorders or diseases (e.g., by conversion of target adenosine to inosine to introduce A to G variation, etc.). In some embodiments, the present disclosure provides methods for preventing or treating a condition, disorder, or disease, comprising administering to a subject susceptible thereto or suffering therefrom an effective amount of a provided oligonucleotide or composition. In some embodiments, the present disclosure provides methods for preventing or treating a condition, disorder, or disease, comprising administering to a subject susceptible to or suffering from a condition, disorder or disease a provided single-stranded oligonucleotide for site-directed editing of a nucleotide (e.g. target adenosine) in a target RNA sequence (e.g., target PNPLA3 RNA sequence), or a composition thereof. In some embodiments, a provided single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequence is of a base sequence that partially or fully complementary to a portion of a transcript, which transcript is associated with a condition, disorder, or disease ((e.g., a PNPLA3 transcript). In some embodiments, a base sequence is such that it preferentially binds to a transcript associated with a condition, disorder or disease over other transcripts that are not associated with said condition, disorder, or disease. In some embodiments, a condition, disorder, or disease is associated with a mutation (e.g., PNPLA3 I148M). In some embodiments, a subject is homozygous with respect to the mutation. In some embodiments, a subject is heterozygous with respect to a mutation.

[01049] In some embodiments, a condition, disorder or disease is associated with increased level and/or

activity of a transcript and/or an encoded product thereby, and a provided technology can reduce level and/or activity of a transcript and/or an encoded product thereby, e.g., through introducing one or more A to I to a transcript. In some embodiments, a condition, disorder or disease is associated with decreased level and/or activity of a transcript and/or an encoded product thereby, and a provided technology can increase level and/or activity of a transcript and/or an encoded product thereby, e.g., through introducing one or more A to I to a transcript. In some embodiments, a condition, disorder or disease is associated with splicing, and a provided technology provides splicing modulation through introducing one or more A to I to a transcript (e.g., pre-mRNA).

[01050] In some embodiments, oligonucleotide compositions in provided methods are chirally controlled oligonucleotide compositions. In some embodiments, a method of treating a condition, disorder or disease can include administering a composition comprising a plurality of oligonucleotides sharing a common base sequence, which base sequence is complementary to a target sequence in a target transcript. Among other things, the present disclosure provides an improvement that comprises administering as the oligonucleotide composition a chirally controlled oligonucleotide composition as described in the present disclosure, characterized in that, when it is contacted with the target transcript in a system, adenosine editing of the transcript is improved relative to that observed under a reference condition selected from the group consisting of absence of the composition, presence of a reference composition, and any combinations thereof. In some embodiments, a reference composition is a racemic preparation of oligonucleotides of the same sequence or constitution. In some embodiments, a target transcript is an oligonucleotide transcript.

[01051] Those skilled in the art reading the present disclosure will appreciate that various amino acid codon mutations, e.g., PNPLA3 I148M, a common type of mutation in human genes, may be corrected (e.g., through variation of amino acid codons to restore or introduce functional protein) and thus benefit from provided technologies. In some embodiments, provided technologies may be utilized to target mutations associated with various polar or charged amino acids (e.g., Ser, Tyr, Asp, Glu, His, Asn, Gln, Lys, etc.), stop codons (opal, ochre and amber), transcriptional start sites, splicing signals, microRNA recognition sites, repetitive elements, microRNAs (miRNAs), protein encoding transcripts, etc. Among other things, provided technologies can elicit diverse functional outcomes, e.g., altered splicing, restored/improved protein expression and/or functions, etc.

[01052] In some embodiments, technologies of the present disclosure provide editing such as A to I editing in nucleic acids like mRNA and can change properties, structures, functions, etc. of amino acid residues, e.g., size, polarity, charge, etc. in polypeptides encoded thereby and can modulate properties, structures, functions, activity levels, etc. of polypeptides. For example, in some embodiments, editing reduces polarity of a side chain. In some embodiments, editing removes a charged size chain. In some embodiments, editing removes an acidic side chain (e.g., from Glu to Gly). In some embodiments, editing removes a basic side chain (e.g., from Arg to Gly). In some embodiments, editing removes a non-polar side chain. In some embodiments, editing removes a side chain with an aromatic group. In some embodiments, editing reduces size of a size chain. In some embodiments, editing increases polarity of a size chain. In some embodiments, editing

increases a charged size chain. In some embodiments, editing introduces an acidic side chain. In some embodiments, editing introduces a basic side chain. In some embodiments, editing introduces a non-polar side chain. In some embodiments, editing introduces a side chain with an aromatic group. In some embodiments, editing increases size of a side chain. In some embodiments, editing reduces size of a side chain. In some embodiments, editing reduces steric hindrance of a side chain. Those skilled in the art appreciate that through modulating properties of amino acid residues, various properties, functions, structures, etc. of polypeptides, e.g., stability, localization, processing, folding, interactions, modifications, etc. can be independently modulated, including independently enhancing, reducing and/or maintaining at comparable levels of various properties, functions, structures, etc., and in some embodiments, new properties, functions, structures, etc. may be introduced.

[01053] In some embodiments, through editing provided technology can restore protein functions (e.g., fix nonsense and missense mutations that cannot be splice-corrected, remove stop mutations, prevent protein misfolding and aggregation, etc., and can be utilized for preventing and/or treating various conditions, disorders or diseases such as recessive or dominant genetically defined diseases), modify protein functions (e.g., alter protein processing (e.g., protease cleavage sites), protein-protein interactions, modulate signaling pathways, etc., and can be utilized for preventing and/or treating various conditions, disorders or diseases such as those related to ion channel permeability), protein upregulation (e.g., miRNA target site modification, modifying upstream ORFs, modification of ubiquitination sites, etc., and can be utilized for preventing and/or treating various conditions, disorders or diseases such as haploinsufficient diseases)). In some embodiments, a provided technology restores or improves expression, level, function and/or activity of a protein. In some embodiments, a condition, disorder or disease is a liver condition, disorder or disease (e.g., hepatocellular carcinoma (HCC)). In some embodiments, a condition, disorder or disease is a metabolic liver condition, disorder or disease. In some embodiments, a provided technology modify express, level, function and/or activity of a protein. In some embodiments, a provided technology reduces express, level, function and/or activity of a protein. In some embodiments, a provided technology increases express, level, function and/or activity of a protein. In some embodiments, a condition, disorder or disease is recessive or dominant genetically defined diseases. In some embodiments, a condition, disorder or disease is a cardiovascular condition, disorder or disease. In some embodiments, a condition, disorder or disease is a cardiometabolic condition, disorder or disease. In some embodiments, a condition, disorder or disease is cancer. In some embodiments, a condition, disorder or disease is an immunological condition, disorder or disease. In some embodiments, a provided technology modifies a modification site of a protein, e.g., a ubiquitination site. In some embodiments, a provided technology is useful for preventing or treating a condition, disorder or disease associated with haploinsufficiency. In some embodiments, a provided technology is useful for preventing or treating a neuronal condition, disorder or disease. In some embodiments, a provided technology is useful for preventing or treating dementias. In some embodiments, a provided technology is useful for preventing or treating a haploinsufficient condition, disorder or disease. In some embodiments, the provided technology

provides a method for prevent or treating a condition, disorder or disease, comprising administering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or a composition thereof as described herein. Those skilled in the art appreciate that through, e.g., editing a nucleobase such as A in a RNA, a protein encoded thereby can be edited. In some embodiments, an amino acid residue is replaced with another amino acid residue. In some embodiments, expression, level, function, stability, property and/or activity are modulated. In some embodiments, some properties and/or activities are enhanced while others are reduced or maintained the same. In some embodiments, some properties and/or activities are reduced while others are enhanced or maintained the same.

[01054] In some embodiments, provided technology edits a nucleic acid or a codon comprising a mutation. In some embodiments, a mutation is a nonsense mutation. In some embodiments, a mutation is a missense mutation. In some embodiments, a mutation is a silent mutation. In some embodiments, a provided technology fixes a nonsense mutation. In some embodiments, a provided technology fixes a missense mutation. In some embodiments, a provided technology removes a stop mutation. In some embodiments, a provided technology prevents or reduces misfolding and/or aggregation. In some embodiments, a provided technology edits a codon comprising a mutation. In some embodiments, an edited nucleobase is a mutation. In some embodiments, an edited nucleobase is not a mutation but another nucleobase in a codon. In some embodiments, after editing a codon becomes its corresponding wild type codon. In some embodiments, after editing a codon encodes the same amino acid as a wild type codon. In some embodiments, after editing a codon encodes a different amino acid from a wild type codon. In some embodiments, a protein comprising such a different amino acid residue shares one or more properties and/or performs one or more functions of its corresponding wild type protein. In some embodiments, a protein comprising such a different amino acid residue shares more similarities to a wild type protein, and/or provides higher levels of desired activities compared to a corresponding mutated, un-edited protein. In some embodiments, a nonsense or missense mutation cannot be splice-corrected. In some embodiments, a provided technology creates a silent mutation. In some embodiments, a silent mutation modulates levels of an encoded protein. In some embodiments, a protein level is increased. In some embodiments, a protein level is decreased.

[01055] In some embodiments, a provided technology modifies protein function. In some embodiments, a provided technology changes one or more properties and/or functions of a nucleic acid (e.g., a transcript) and/or a protein. In some embodiments, a provided technology increases, promotes, or enhances one or more properties and/or functions of a nucleic acid (e.g., a transcript) and/or a protein. In some embodiments, a provided technology provide one or more new properties and/or activities, e.g., of a nucleic acid (e.g., a transcript) and/or a protein. In some embodiments, a provided technology decreases, inhibits, or removes one or more properties and/or functions of a nucleic acid (e.g., a transcript) and/or a protein. In some embodiments, a provided technology alter protein processing. In some embodiments, provided technologies edit one or more residues involved in protein-protein interactions. In some embodiments, provided technologies edit amino acid residues at protein-protein interactions domains. In some embodiments, through editing mRNAs that

encode proteins, residues at various regions of polypeptides, e.g., protease cleavage sites, various domains (e.g., protein-protein interactions domains), modification sites, miRNA targeting sites, ubiquitination sites, etc. can be edited. In some embodiments, provided technologies modulate signaling pathways.

[01056] In some embodiments, provided technologies restore, increase or enhance levels of functional proteins. In some embodiments, provided technologies reduce levels and/or activities of mutant or undesired nucleic acids (e.g., RNA transcripts) and proteins. In some embodiments, provided technologies restore or correct expression of one or more polypeptides. In some embodiments, provided technologies can upregulate expression. In some embodiments, provided technologies can upregulate translation. In some embodiments, provided technologies can upregulate activity levels of polypeptides. In some embodiments, provided technologies modify functions of target nucleic acids (e.g., RNA transcripts) and/or products encoded thereby (e.g., polypeptides). In some embodiments, provided technologies modulate post-translation modifications of target nucleic acids (e.g., RNA transcripts) and/or products encoded thereby (e.g., polypeptides). In some embodiments, provided technologies can upregulate levels of polypeptides. In some embodiments, provided technologies edit codons encoding amino acid residues involved in protein-protein interactions or protein interactions with other agents, including in some embodiments, changing the amino acid residues to different amino acid residues to enhance or reduce interactions. In some embodiments, provided technologies modify one or more functions of nucleic acids and/or proteins. In some embodiments, provided technologies can modulate protein-protein interactions. In some embodiments, provided technologies edit encoding transcripts to remove, change, or incorporate amino acid residues for post-translation modification. In some embodiments, provided technologies modulate post-translational modifications. In some embodiments, provided technologies modulate nucleic acid folding. In some embodiments, provided technologies modulate protein folding. In some embodiments, provided technologies modulate stability of transcripts and/or products thereof. In some embodiments, provided technologies modulate protein stability. In some embodiments, provided technologies modulate processing of transcripts and/or products thereof. In some embodiments, provided technologies modulate nucleic acids (e.g., transcripts) processing. In some embodiments, provided technologies alter protein processing. In some embodiments, provided technologies modulate post translational processes. In some embodiments, provided technologies modulate localization of an agent, e.g., RNA, polypeptide, etc. In some embodiments, provided technologies modulate polypeptide localization. Among other things, provided technologies are applicable to a wide range of therapeutic applications with large patient populations.

[01057] Among other things, the present disclosure provides technologies for preventing and/or treating various diseases, disorders, or conditions. In some embodiments, a disease, disorder, or condition is an inherited disease, disorder, or condition.

[01058] Those skilled in the art reading the present disclosure appreciate that by editing amino acid residues in polypeptides, e.g., through editing corresponding encoding RNA nucleic acids, interactions of polypeptides with various agents (e.g., polypeptides, nucleic acids, lipids, carbohydrates, small molecules, etc.)

can be modulated. In some embodiments, editing can enhance interactions. In some embodiments, editing can reduce interactions. In some embodiments, for a polypeptide interactions may be modulated independently, for example, an interaction may be enhanced, an interaction may be reduced, and/or an interaction may be maintained at a comparable level.

[01059] In some embodiments, one or more amino acid residues of one or more proteins may be changed through editing of encoding mRNAs to modulate protein-protein interactions. Suitable amino acid residues for editing include various reported amino acid residues involved in protein-protein interactions, or can be identified through technologies available in the art, e.g., mutation technologies, structural biology technologies, etc. In some embodiments, the present disclosure provides technologies for modulating levels, properties and/or activities of nucleic acids (e.g., transcripts) and/or proteins through editing of nucleic acids (e.g., transcripts) and/or proteins that interact them. In some embodiments, the present disclosure provides technologies for modulating levels and/or activities of a protein (e.g., a transcription factor) and/or transcription and/or expression regulated thereby. In some embodiments, a provided technology comprises editing an amino acid residue of a protein (e.g., a transcription factor) or a partner protein that it interacts with, wherein interaction between the protein and a partner protein is reduced or enhanced. In some embodiments, a provided technology comprises editing an amino acid residue of a protein (e.g., a transcription factor) or a partner protein that it interacts with, wherein interaction between the protein and a partner protein is reduced. In some embodiments, such editing stabilizes a protein so that its levels and/or activities (e.g., transcription activation of certain nucleic acids) are increased. In some embodiments, the present disclosure provides technologies for modulating (e.g., activating, increasing, reducing, suppressing, etc.) expression of a nucleic acid, comprising editing an adenosine in a transcript encoding a protein that regulates expression of the nucleic acid, or a protein that interacts with a protein that regulates expression of the nucleic acid, or a protein that is a member of a pathway comprising a protein that regulates expression of the nucleic acid, wherein editing modulates levels and/or activities of a protein that regulates expression of the nucleic acid. In some embodiments, transcripts levels and/or activities of a nucleic acids are modulated. In some embodiments, levels and/or activities of proteins encoded by such transcripts are modulated. Among other things, the present disclosure confirms that many functions, activities, pathways, etc., that involve protein-protein interactions may be modulated through editing of interacting amino acid residues of one or more interacting proteins.

[01060] In some embodiments, provided technologies modulate enzymatic activities. In some embodiments, provided technologies increase an enzymatic activity, e.g., through editing a codon to a codon encoding an amino acid residue that can increase an enzymatic activity. In some embodiments, provided technologies decrease an enzymatic activity, e.g., those associated with a condition, disorder or disease, through editing a codon to a codon encoding an amino acid residue that can decrease an enzymatic activity. Various enzymatic activities, in many cases with amino acid residues involved for such activities, are reported or can be identified and characterized, and can be modulated in accordance with the present disclosure. In some embodiments, an activity is a lipase activity. In some embodiments, the present disclosure provides

methods for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof. In some embodiments, a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof comprises modifying an amino acid residue at a position that is or corresponds to position 148 of SEQ ID NO: 2. In some embodiments, a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof comprises modifying an amino acid residue of the PNPLA3 polypeptide or characteristic portion thereof at a position that is or corresponds to position 148 of SEQ ID NO: 2. In some embodiments, an amino acid residue is methionine. In some embodiments, an amino acid residue is isoleucine. In some embodiments, an amino acid residue is modified to be valine. In some embodiments, increased lipase activity is about or at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 fold of that without the modification. In some embodiments, lipase activity is increased as compared to that of a PNPLA3 polypeptide comprising M148. In some embodiments, lipase activity is comparable to that of a PNPLA3 polypeptide comprising I148.

[01061] In some embodiments, editing of a protein (e.g., through editing of its encoding mRNA to change one or more amino acid residues) decreases degradation of the protein or a protein which it interacts with. In some embodiments, editing of a protein upregulate its levels. In some embodiments, editing of a protein modulate protein processing. In some embodiments, editing of a protein modulate its folding. In some embodiments, editing of a protein modulate its stability. In some embodiments, editing of a protein modulate protein modification (e.g., increasing, decreasing, removing or introducing a modification site, etc.). In some embodiments, editing of a protein modulate post-translational modification (e.g., increasing, decreasing, removing or introducing a modification site, etc.). In some embodiments, provided technologies are useful for treating associated conditions, disorders or diseases, such as dementias, familial epilepsies, neuropathic pain, neuromuscular disorders, dementias, haploinsufficient diseases, loss of function conditions, disorders or diseases, etc.

[01062] As described herein, technologies described herein may be utilized to modulate expression. In some embodiments, the present disclosure provides methods for modulating level of a nucleic acid and/or a product encoded by, comprising contacting the nucleic acid with an oligonucleotide or an oligonucleotide composition described herein. As described herein, various technologies described herein can modify an A in a nucleic acid. In some embodiments, an A is modified so that if the nucleic acid is translated, it is translated as G. In some embodiments, an A is modified into I. In some embodiments, the present disclosure provides technologies for upregulating expression. In some embodiments, the present disclosure provides technologies for increasing level of a nucleic acid (e.g., a transcript) and/or a product encoded thereby. In some embodiments, the present disclosure provides methods for downregulating expression. In some embodiments, the present disclosure provides technologies for reducing level of a nucleic acid (e.g., a transcript) and/or a product encoded thereby. In some embodiments, a nucleic acid is a RNA nucleic acid. In some embodiments, a nucleic acid is mRNA. In some embodiments, a nucleic acid is RNA encoding a polypeptide. In some embodiments, a nucleic acid is RNA encoding a protein. Without intention to be limited by any particular

theory, Applicant notes that expression modulation may be achieved through various potential mechanisms; for example, in some embodiments, after A to I modification, a nucleic acid such as RNA may be more stable, and/or can be processed and/or translated more efficiently so that expression of the nucleic acid and/or a product encoded thereby can be upregulate; in some embodiments, after A to I modification, a nucleic acid such as RNA may be less stable, and/or can be processed and/or translated less efficiently so that expression of the nucleic acid and/or a product encoded thereby can be downregulated.

[01063] In some embodiments, technologies herein modulate activities of nucleic acids (e.g., RNA such as various transcripts). In some embodiments, technologies herein increase level of an activity of a nucleic acid (e.g., RNA such as various transcripts). In some embodiments, technologies herein decrease level of an activity of a nucleic acid (e.g., RNA such as various transcripts). In some embodiments, an activity is a new activity which is not observed prior to adenosine editing. In some embodiments, editing of target adenosines can modulate interactions of nucleic acids (e.g., RNA such as various transcripts) with other agents, e.g., nucleic acids, polypeptides, etc. In some embodiments, interactions are enhanced. In some embodiments, interactions are reduced. Those skilled in the art appreciate that in some embodiments, for a nucleic acid interactions can be independently modulated. In some embodiments, for interaction between a nucleic acid and an interacting agent, in some circumstances it may be enhanced while in other circumstances it may be reduced or maintained at comparable levels. In some embodiments, an interaction is not observed prior to adenosine editing. In some embodiments, adenosines in functional motifs are edited. Those skilled in the art appreciate that various functional motifs have been reported, and various tools have been developed and/or can be developed to identify functional motifs. In some embodiments, technologies herein are utilized to edit adenosines in various functional motifs to modulate properties, structures, functions, activity levels, etc. of various nucleic acids comprising such functional motifs.

[01064] In some embodiments, technologies described herein can edit N^6-methyladenosines (m^6A). In some embodiments, a m^6A is present in a consensus sequence of RRACH (R = A/G, H = U/A/C). In some embodiments, m^6A editing modulates properties, structures, functions, activity levels, etc. of m^6A and/or nucleic acids comprising m^6A (e.g., a gene comprising m^6A). Among other things, ARE motifs have been reported to modulate mRNA metabolism and regulate various biological processes, including, e.g., gene expression. m^6A has been reported to be the most prevalent modification in mRNA in higher eukaryotes. m^6A modification is reported to be catalyzed by the METTL3 and METTL4 methyltransferase complex and removed by demethylases FTO and ALKBH5. In some embodiments, adenosine editing of m^6A may modulate RNA/protein interactions. In some embodiments, provided technologies can reduce m^6A levels at targeted locations.

[01065] In some embodiments, provided technologies edit RNA motifs that interact with polypeptides, e.g., RNA binding proteins, to modulate RNA properties, structures, functions, activity levels, etc. and/or modulate gene regulation. For example, in some embodiments, provided technologies can modulate RNA processing (e.g., splicing, polyA usage, capping, etc.), transport (e.g., intracellular localization), stability (e.g.,

inhibiting or enhancing mRNA decay), protein production (e.g., translational efficiency), etc.

[01066] Technologies of present disclosure can provide efficient editing in various types of cells, tissues, organs and/or organisms. In some embodiments, provided technologies can provide efficient editing in various immune cells. Provided technologies can provide high levels of editing in human peripheral blood mononuclear cells (PBMCs). Among other things, provided technologies can provide high levels of editing in various cell populations such as CD4+ T cells, CD8+ T cells, CD14 monocytes, CD19 B cells, NK cells, Tregs T cells, etc. In some embodiments, immune cells are activated (e.g., by PHA) before contact with oligonucleotides. In some embodiments, cells are non-activated. In some embodiments, similar levels of editing are observed in activated and non-activated cells. In some embodiments, higher levels of editing are observed in activated cells. In some embodiments, after editing cells, e.g., PBMCs, may be sorted into various cell types. In some embodiments, cells can be first sorted before contact with oligonucleotides. As appreciated by those skilled in the art, immune cells have a number of functions and may be utilized for a number of purposes including for treating various conditions, disorders or diseases. In some embodiments, immune cells are utilized in immunotherapy, e.g., for various types of cancer. Among other things, the present disclosure provides technologies for editing one or more transcripts expressed in immune cells to improve its properties and/or activities for immunotherapy. In some embodiments, provided technologies can reduce expression and/or activity of one or more genes in immune cells, e.g., FAS, BID, CTLA4, PDCD1, CBLB, PTPN6, TRAC, TRBC, etc. In some embodiments, transcripts from such genes are edited. In some embodiments, a target cell is a T cell, e.g., a CD8+ T cell (e.g., a CD8+ naïve T cell, central memory T cell, or effector memory T cell), a CD4+ T cell, a natural killer T cell (NK T cell), a regulatory T cell (Treg), a stem cell memory T cell, a lymphoid progenitor cell, a hematopoietic stem cell, a natural killer cell (NK cell) or a dendritic cell. In some embodiments, cells are CD4+ cells, e.g., CD4+ T cells. In some embodiments, cells are CD8+ cells, e.g., CD8+ T cells. In some embodiments, cells are CD14+ cells, e.g., CD14+ monocytes. In some embodiments, cells are CD19+ cells, e.g., CD19+ B cells. In some embodiments, cells are NC cells. In some embodiments, cells are T-regulatory cells. In some embodiments, a target cell is an induced pluripotent stem (iPS) cell or a cell derived from an iPS cell, e.g., an iPS cell generated from a subject, manipulated to alter (e.g., induce a mutation in) expression of one or more genes, e.g., FAS, BID, CTLA4, PDCD1, CBLB, PTPN6, TRAC or TRBC gene, and differentiated into, e.g., a T cell, e.g., a CD8+ T cell (e.g., a CD8+ naïve T cell, central memory T cell, or effector memory T cell), a CD4+ T cell, a stem cell memory T cell, a lymphoid progenitor cell or a hematopoietic stem cell.

[01067] Among other things, provided technologies are useful for increasing, enhancing, improving or upregulating levels, properties, activities, etc., of various polypeptides including various proteins. In some embodiments, provided technologies modify binding or target sites, e.g., miRNA target sites. In some embodiments, provided technologies modify regulatory elements in transcripts. In some embodiments, provided technologies modify upstream ORFs (e.g., A in ATG). In some embodiments, provided technologies modify amino acid residues that can be modified, e.g., ubiquitination sites. Those skilled in the art appreciate

provided technologies can also be useful for decreasing or downregulating levels, properties, activities, etc., of various polypeptides including various proteins through modifying RNAs.

[01068] In some embodiments, an editing site, e.g., a target adenosine, is in a coding region. In some embodiments, it is in a non-coding region. In some embodiments, a target nucleic acid is a non-coding RNA.

[01069] Certain applications are described, e.g., in WO 2016/097212, WO 2017/220751, WO 2018/041973, WO 2018/134301A1, WO 2020/154344, WO 2020/154343, WO 2020/154342, WO 2020/165077, WO 2020/201406, WO 2020/216637, WO 2020/252376, WO 2021/130313, WO 2021/231673, WO 2021/231675, WO 2021/231679, WO 2021/231680, WO 2021/231685, WO 2021/231691, WO 2021/231692, WO 2021/231698, WO 2021/231830, WO 2021/243023, WO 2022/018207, or WO 2022/026928.

[01070] In some embodiments, when an oligonucleotide or oligonucleotide composition is contacted with a target nucleic acid comprising a target adenosine in a system, a target adenosine in a target nucleic acid is modified. In some embodiments, when an oligonucleotide or oligonucleotide composition is contacted with a target nucleic acid comprising a target adenosine in a system, level of a target nucleic acid is reduced compared to absence of the product or presence of a reference oligonucleotide. In some embodiments, when an oligonucleotide or oligonucleotide composition is contacted with a target nucleic acid comprising a target adenosine in a system, splicing of a target nucleic acid or a product thereof is altered compared to absence of the oligonucleotide or presence of a reference oligonucleotide. In some embodiments, when an oligonucleotide or oligonucleotide composition is contacted with a target nucleic acid comprising a target adenosine in a system, level of a product of a target nucleic acid is altered compared to absence of the product or presence of a reference oligonucleotide. In some embodiments, level of a product is increased, wherein the product is or is encoded by a nucleic acid which is otherwise identical to a target nucleic acid but a target adenosine is modified. In some embodiments, level of a product is increased, wherein the product is or is encoded by a nucleic acid which is otherwise identical to a target nucleic acid but a target adenosine is replaced with inosine. In some embodiments, level of a product is increased, wherein the product is or is encoded by a nucleic acid which is otherwise identical to a target nucleic acid but the adenine of a target adenosine is replaced with guanine. In some embodiments, a product is a protein. In some embodiments, a target adenosine is more associated with a condition, disorder or disease than a guanine at the same position. In some embodiments, an oligonucleotide is capable of forming a double-stranded complex with a target nucleic acid. In some embodiments, a target nucleic acid or a portion thereof is or comprises RNA. In some embodiments, a target adenosine is of an RNA. In some embodiments, a target adenosine is modified, and the modification is or comprises deamination of a target adenosine. In some embodiments, a target adenosine is modified and the modification is or comprises conversion of a target adenosine to an inosine. In some embodiments, a modification is promoted by an ADAR protein. In some embodiments, a system is an *in vitro* or *ex vivo* system comprising an ADAR protein. In some embodiments, a system is or comprises a cell that comprises or expresses an ADAR protein. In some embodiments, a system is a subject comprising a cell that comprises or

expresses an ADAR protein. In some embodiments, a ADAR protein is ADAR1. In some embodiments, an ADAR1 protein is or comprises p110 isoform. In some embodiments, an ADAR1 protein is or comprises p150 isoform. In some embodiments, an ADAR1 protein is or comprises p110 and p150 isoform. In some embodiments, a ADAR protein is ADAR2. As demonstrated herein, the present disclosure among other things provides technologies for recruiting enzymes to target sites (e.g., those comprising target As), comprising contacting such target sites with, or administering to systems comprising or expressing polynucleotide (e.g., RNA) comprising such target sites, provided oligonucleotides or compositions thereof. In some embodiments, an enzyme is an RNA-editing enzyme such as ADAR1, ADAR2, etc. as described herein.

[01071] In some embodiments, an oligonucleotide composition comprising a plurality of oligonucleotides provide a greater level, e.g., a target adenosine is modified at a greater level, than that is observed with a comparable reference oligonucleotide composition. In some embodiments, a reference oligonucleotide composition comprises no or a lower level of oligonucleotides of the plurality. In some embodiments, a reference composition does not contain oligonucleotides that have the same constitution as an oligonucleotide of the plurality. In some embodiments, a reference composition does not contain oligonucleotides that have the same structure as an oligonucleotide of the plurality. In some embodiments, a reference oligonucleotide composition is a composition whose oligonucleotides having the same base sequence as oligonucleotides of the plurality contain a lower level of 2'-F modifications compared to oligonucleotides of the plurality. In some embodiments, a reference oligonucleotide composition is a composition whose oligonucleotides having the same base sequence as oligonucleotides of the plurality contain a lower level of 2'-OMe modifications compared to oligonucleotides of the plurality. In some embodiments, a reference oligonucleotide composition is a composition whose oligonucleotides having the same base sequence as oligonucleotides of the plurality have a different sugar modification pattern compared to oligonucleotides of the plurality. In some embodiments, a reference oligonucleotide composition is a composition whose oligonucleotides having the same base sequence as oligonucleotides of the plurality contain a lower level of modified internucleotidic linkages compared to oligonucleotides of the plurality. In some embodiments, a reference oligonucleotide composition is a composition whose oligonucleotides having the same base sequence as oligonucleotides of the plurality contain a lower level of phosphorothioate internucleotidic linkages compared to oligonucleotides of the plurality. In some embodiments, a composition is a stereorandom oligonucleotide composition. In some embodiments, a reference composition is a stereorandom oligonucleotide composition of oligonucleotides of the same constitution as oligonucleotides of the plurality.

[01072] In some embodiments, the present disclosure provides technologies for modifying a target adenosine in a target nucleic acid, comprising contacting a target nucleic acid with an provided oligonucleotide or oligonucleotide composition as described herein. In some embodiments, the present disclosure provides a method for deaminating a target adenosine in a target nucleic acid, comprising contacting a target nucleic acid with an oligonucleotide or composition as described herein. In some embodiments, the present disclosure provides a method for producing, or restoring or increasing level of a product of a particular nucleic acid,

comprising contacting a target nucleic acid with a provided oligonucleotide or composition wherein a target nucleic acid comprises a target adenosine, and the particular nucleic acid differs from a target nucleic acid in that the particular nucleic acid has an I or G instead of a target adenosine. In some embodiments, the present disclosure provides a method for reducing level of a product of a target nucleic acid, comprising contacting a target nucleic acid with an oligonucleotide or composition of the present disclosure, wherein a target nucleic acid comprises a target adenosine. In some embodiments, a product is a protein. In some embodiments, a product is a mRNA.

[01073] In some embodiments, the present disclosure provides a method, comprising:

contacting an oligonucleotide or composition with a sample comprising a target nucleic acid and an adenosine deaminase, wherein:

the base sequence of the oligonucleotide or oligonucleotides in the oligonucleotide composition is substantially complementary to that of a target nucleic acid; and

a target nucleic acid comprises a target adenosine;

wherein a target adenosine is modified.

[01074] In some embodiments, the present disclosure provides a method comprising:

1) obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid; and

2) obtaining a reference level of modification of a target adenosine in a target nucleic acid, which level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise more sugars with 2'-F modification, more sugars with 2'-OR modification wherein R is not −H, and/or more chiral internucleotidic linkages than oligonucleotides of the reference plurality; and

the first oligonucleotide composition provides a higher level of modification compared to oligonucleotides of the reference oligonucleotide composition.

[01075] In some embodiments, the present disclosure provides a method comprising:

obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target

nucleic acid; and

wherein the first level of modification of a target adenosine is higher than a reference level of modification of a target adenosine, wherein the reference level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise more sugars with 2'-F modification, more sugars with 2'-OR modification wherein R is not –H, and/or more chiral internucleotidic linkages than oligonucleotides of the reference plurality.

[01076] In some embodiments, the present disclosure provides a method comprising:

1) obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid; and

2) obtaining a reference level of modification of a target adenosine in a target nucleic acid, which level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise more sugars with 2'-F modification, more sugars with 2'-OR modification wherein R is not –H, and/or more chirally controlled chiral internucleotidic linkages than oligonucleotides of the reference plurality; and

the first oligonucleotide composition provides a higher level of modification compared to oligonucleotides of the reference oligonucleotide composition.

[01077] In some embodiments, the present disclosure provides a method comprising:

obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid; and

wherein the first level of modification of a target adenosine is higher than a reference level of modification of a target adenosine, wherein the reference level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase,

wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise more sugars with 2'-F modification, more sugars with 2'-OR modification wherein R is not −H, and/or more chirally controlled chiral internucleotidic linkages than oligonucleotides of the reference plurality.

[01078] In some embodiments, the present disclosure provides a method comprising:

1) obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid; and

2) obtaining a reference level of modification of a target adenosine in a target nucleic acid, which level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise one or more chirally controlled chiral internucleotidic linkages; and

oligonucleotides of the reference plurality comprise no chirally controlled chiral internucleotidic linkages (a reference oligonucleotide composition is a "stereorandom composition); and

the first oligonucleotide composition provides a higher level of modification compared to oligonucleotides of the reference oligonucleotide composition.

[01079] In some embodiments, the present disclosure provides a method comprising:

obtaining a first level of modification of a target adenosine in a target nucleic acid, which level is observed when a first oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the first oligonucleotide composition comprises a first plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid; and

wherein the first level of modification of a target adenosine is higher than a reference level of modification of a target adenosine, wherein the reference level is observed when a reference oligonucleotide composition is contacted with a sample comprising a target nucleic acid and an adenosine deaminase, wherein the reference oligonucleotide composition comprises a reference plurality of oligonucleotides sharing the same base sequence which is substantially complementary to that of a target nucleic acid;

wherein:

oligonucleotides of the first plurality comprise one or more chirally controlled chiral internucleotidic linkages; and

oligonucleotides of the reference plurality comprise no chirally controlled chiral internucleotidic linkages (a reference oligonucleotide composition is a "stereorandom composition).

[01080] In some embodiments, a first oligonucleotide composition is an oligonucleotide composition as described herein. In some embodiments, a first oligonucleotide composition is a chirally controlled oligonucleotide composition. In some embodiments, a deaminase is an ADAR enzyme. In some embodiments, a deaminase is ADAR1. In some embodiments, a deaminase is ADAR2. In some embodiments, a sample is or comprise a cell. In some embodiments, a target nucleic acid is more associated with a condition, disorder or disease, or decrease of a desired property or function, or increase of an undesired property or function, compared to a nucleic acid which differs from a target nucleic acid in that it has an I or G at the position of a target adenosine instead of a target adenosine.

[01081] Among other things, oligonucleotide designs of the present disclosure, e.g., nucleobase, sugar, internucleotidic linkage modifications, control of linkage phosphorus stereochemistry, and/or patterns thereof, can be applied to improve prior technologies. In some embodiments, the present disclosure provides improvement over prior technologies by introducing one or more structural features of the present disclosure, e.g., nucleobase, sugar, internucleotidic linkage modifications, control of linkage phosphorus stereochemistry, and/or patterns thereof to oligonucleotides in prior technologies. In some embodiments, an improvement is or comprises improvement from control of linkage phosphorus stereochemistry.

[01082] In some embodiments, the present disclosure provides technologies for improving adenosine editing by a polypeptide, e.g., ADAR1, ADAR2, etc., comprising incorporating into an oligonucleotide a design (e.g., one or more modifications and/or patterns thereof) as described herein. In some embodiments, a design is or comprises a modified base as described herein, e.g., at the position opposite to a target adenosine and/or one or both of its neighboring positions. In some embodiments, a design is or comprises one or more sugar modifications and/or patterns thereof, one or more base modifications and/or patterns thereof, one or more modified internucleotidic linkages and/or patterns thereof, and/or controlled stereochemistry at one or more positions and/or patterns thereof. In some embodiments, a provided technology improves editing by ADAR1 more than ADAR2. In some embodiments, a provided technology improves editing by ADAR2 more than ADAR1. In some embodiments, a provided technology improves editing by ADAR1 p110 more than p150 (e.g., in some embodiments, *R*p (e.g., of phosphorothioate internucleotidic linkages) at one or more positions). In some embodiments, a provided technology improves editing by ADAR1 p150 more than p110.

[01083] In some embodiments, a provided technology comprises increasing levels of an adenosine editing polypeptide, e.g., ADAR1 (p110 or p150) or ADAR2, or a portion thereof. In some embodiments, an increase is through expression of an exogenous of a polypeptide.

[01084] In some embodiments, a provided oligonucleotide or oligonucleotide composition does not cause significant degradation of a nucleic acid (e.g., no more than about 5%-100% (e.g., no more than about 10%-

100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.)). In some embodiments, a composition does not cause significant undesired exon skipping or altered exon inclusion in a target nucleic acid (e.g., no more than about 5%-100% (e.g., no more than about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.)).

[01085] In some embodiments, provided technologies can provide high levels of adenosine editing (e.g., conversion to inosine). In some embodiments, percentage of target adenosine editing is about 10%-100%, e.g., at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, or 95%. In some embodiments, it is at least 10%. In some embodiments, it is at least 15%. In some embodiments, it is at least 20%. In some embodiments, it is at least 25%. In some embodiments, it is at least 30%. In some embodiments, it is at least 35%. In some embodiments, it is at least 40%. In some embodiments, it is at least 45%. In some embodiments, it is at least 50%. In some embodiments, it is at least 60%. In some embodiments, it is at least 70%. In some embodiments, it is at least 75%. In some embodiments, it is at least 80%. In some embodiments, it is at least 85%. In some embodiments, it is at least 90%. In some embodiments, it is at least 95%. In some embodiments, it is at least about 100%.

[01086] In some embodiments, an oligonucleotide or a composition thereof is capable of mediating a decrease in the expression or level of a target nucleic acid or a product thereof (e.g., by modifying a target adenosine into inosine). In some embodiments, an oligonucleotide or a composition thereof is capable of mediating a decrease in the expression or level of a target gene or a gene product thereof (e.g., by modifying a target adenosine into inosine) in a cell in vitro. In some embodiments, expression or level can be decreased by at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, or 95%. In some embodiments, expression or level of a target gene or a gene product thereof can be decreased by at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, or 95% by ADAR-mediated deamination directed by an oligonucleotide or a composition thereof, e.g., at a concentration of 10 uM or less in a cell(s) in vitro. In some embodiments, an oligonucleotide or a composition thereof is capable of provide suitable levels of activities at a concentration of 1 nM, 5 nM, 10 nM or less (e.g., when assayed in cells in vitro or in vivo).

[01087] In some embodiments, activity of provided oligonucleotides and compositions may be assessed by IC50, which is the inhibitory concentration to decrease level of a target nucleic acid or a product thereof

by 50% in a suitable condition, e.g., cell-based in vitro assays. In some embodiments, provided oligonucleotides or compositions have an IC50 no more than 0.001, 0.01, 0.1, 0.5, 1, 2, 5, 10, 50, 100, 200, 500 or 1000 nM, e.g., when assessed in cell-based assays. In some embodiments, an IC50 is no more than about 500 nM. In some embodiments, an IC50 is no more than about 200 nM. In some embodiments, an IC50 is no more than about 100 nM. In some embodiments, an IC50 is no more than about 50 nM. In some embodiments, an IC50 is no more than about 25 nM. In some embodiments, an IC50 is no more than about 10 nM. In some embodiments, an IC50 is no more than about 5 nM. In some embodiments, an IC50 is no more than about 2 nM. In some embodiments, an IC50 is no more than about 1 nM. In some embodiments, an IC50 is no more than about 0.5 nM.

[01088] In some embodiments, provided technologies can provide selective editing of target adenosine over other adenosine residues in a target adenosine. In some embodiments, selectivity of a target adenosine over a non-target adenosine is at least 1.5, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 40, 50, 60, 70, 80, 90, 100 fold or more (e.g., as measured by level of editing of a target adenosine over a non-target adenosine at a suitable condition, or by oligonucleotide concentrations for a certain level of editing (e.g., 0.5%, 1%, 2%, 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, etc.). In some embodiments, a selectivity is at least 2 fold. In some embodiments, a selectivity is at least 3 fold. In some embodiments, a selectivity is at least 4 fold. In some embodiments, a selectivity is at least 5 fold. In some embodiments, a selectivity is at least 10 fold. In some embodiments, a selectivity is at least 25 fold. In some embodiments, a selectivity is at least 50 fold. In some embodiments, a selectivity is at least 100 fold.

[01089] In some embodiments, the present disclosure provides a method for suppression of a transcript from a target nucleic acid sequence for which one or more similar nucleic acid sequences exist within a population, each of the target and similar sequences contains a specific characteristic sequence element that defines the target sequence relative to the similar sequences, the method comprising contacting a sample comprising transcripts of target nucleic acid sequence with an oligonucleotide , or a composition comprising a plurality of oligonucleotides sharing a common base sequence, wherein the base sequence of the oligonucleotide, or the common base sequence of the plurality of oligonucleotide, is or comprises a sequence that is complementary to the characteristic sequence element that defines the target nucleic acid sequence. In some embodiments, wherein when the oligonucleotide, or the oligonucleotide composition, is contacted with a system comprising transcripts of both the target nucleic acid sequence and a similar nucleic acid sequences, transcripts of the target nucleic acid sequence are suppressed at a greater level than a level of suppression observed for a similar nucleic acid sequence. In some embodiments, suppression of the transcripts of the target nucleic acid sequence can be 1.1-100, 2-100, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8, 9, or 10-fold greater than suppression observed for a similar nucleic acid sequence. In some embodiments, a target nucleic acid sequence is associated with (or more associated with compared to a similar nucleic acid sequence) a condition, disorder or disease. As those skilled in the art will appreciate, selective reduction of a transcript (and/or products thereof) associated with conditions, disorders or diseases, while maintaining transcripts that are not, or are less,

associated with conditions, disorders or diseases can provide a number of advantages, for example, providing disease treatment and/or prevention while maintaining one or more desired biological functions (which may provide, among other things, fewer or less severe side effects).

[01090] In some embodiments, as demonstrated herein, selectivity is at least 10 fold, or 20, 30, 40, or 50 fold or more in a system, *e.g.* a reporter assay described herein. In some embodiments, an oligonucleotide or composition can effectively reduce levels of mutant protein (*e.g.*, at least 50%, 60%, 70% or more reduction of a mutant protein) while maintaining levels of wild-type protein (*e.g.* at least 70%, 75%, 80%, 85%, 90%, 95%, or more wild-type protein remaining) in a system . In some embodiments, provided oligonucleotides are stable in various biological systems, *e.g.* in mouse brain homogenates (*e.g.*, at least 70%, 75%, 80%, 85%, 90%, 95%, or more remaining after 1, 2, 3, 4, 5, 6, 7, or 8 days). In some embodiments, provided oligonucleotides are of low toxicity. In some embodiments, provided oligonucleotides and compositions thereof, *e.g.*, chirally controlled oligonucleotides and compositions thereof, do not significant activate TLR9 (*e.g.*, when compared to reference oligonucleotides and compositions thereof (*e.g.*, corresponding stereorandom oligonucleotides and compositions thereof)). In some embodiments, provided oligonucleotides and compositions thereof, *e.g.*, chirally controlled oligonucleotides and compositions thereof, do not significantly induce complement activation (*e.g.*, when compared to reference oligonucleotides and compositions thereof (*e.g.*, corresponding stereorandom oligonucleotides and compositions thereof)).

[01091] For various applications, provided oligonucleotides and/or compositions may be provided as pharmaceutical compositions. In some embodiments, the present disclosure provides a pharmaceutical composition comprising a compound and a pharmaceutically acceptable carrier. In some embodiments, a compound is Compound A-1 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound A-2 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound A-3 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound A-4 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound B-1 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound B-2 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound B-3 or a pharmaceutically acceptable salt thereof. In some embodiments, a compound is Compound B-4 or a pharmaceutically acceptable salt thereof. In some embodiments, the present disclosure provides a pharmaceutical composition comprising an oligonucleotide and a pharmaceutically acceptable carrier. In some embodiments, an oligonucleotide is ADR-0110420. In some embodiments, an oligonucleotide is ADR-0110652. In some embodiments, an oligonucleotide is ADR-0110667. In some embodiments, an oligonucleotide is ADR-0110481. In some embodiments, an oligonucleotide is ADR-0111148. In some embodiments, an oligonucleotide is ADR-0111146. In some embodiments, an oligonucleotide is ADR-0111820. In some embodiments, an oligonucleotide is ADR-0111776. In some embodiments, the present disclosure provides a composition which can deliver a compound described herein. In some embodiments, the present disclosure provides a composition which can deliver an oligonucleotide described herein. In some

embodiments, the present disclosure provides a pharmaceutical composition which comprises or delivers an effective amount of an oligonucleotide or a pharmaceutically acceptable salt thereof. In some embodiments, a pharmaceutical composition may comprise various forms of an oligonucleotide, e.g., acid, base and various pharmaceutically acceptable salt forms. In some embodiments, an oligonucleotide or a compound is a pharmaceutically acceptable salt form. In some embodiments, a pharmaceutically acceptable salt is sodium salt. In some embodiments, a pharmaceutically acceptable salt is a potassium salt. In some embodiments, a pharmaceutically acceptable salt is a amine salt (e.g., of an amine having the structure of $N(R)_3$). In some embodiments, a pharmaceutical composition further comprises a pharmaceutically acceptable carrier. In some embodiments, a pharmaceutical composition is or comprises a liquid solution. In some embodiments, a liquid composition has a controlled pH range, e.g., around or being physiological pH. In some embodiments, a pharmaceutical composition comprises or is formulated as a solution in a physiologically compatible buffers such as Hanks's solution, Ringer's solution, cerebral spinal fluid, artificial cerebral spinal fluid (aCSF) or physiological saline buffer. In some embodiments, a pharmaceutical composition is an injectable suspension or solution. In certain embodiments, injectable suspensions or solutions are prepared using appropriate liquid carriers, suspending agents and the like. Pharmaceutical compositions can be administered in various suitable routes. In some embodiments, pharmaceutical compositions are formulated for oral administration, for example, drenches (aqueous or non-aqueous solutions or suspensions), tablets, e.g., those targeted for buccal, sublingual, and systemic absorption, boluses, powders, granules, pastes for application to the tongue; parenteral administration, for example, by subcutaneous, intramuscular, intravenous, intrathecal, intracerebroventricular, intravitreal, subretinal, suprachoroidal or epidural injection as, for example, a sterile solution or suspension, e.g., in physiologically compatible buffers such as Hanks's solution, Ringer's solution, artificial cerebral spinal fluid (aCSF) or physiological saline buffer or sustained-release formulation; topical application, for example, as a cream, ointment, or a controlled-release patch or spray applied to the skin, lungs, or oral cavity; intravaginally or intrarectally, for example, as a pessary, cream, or foam; sublingually; ocularly; transdermally; or nasally, pulmonary, and to other mucosal surfaces. In some embodiments, technologies herein provide various delivery advantages, e.g., high delivery efficiency, delivery without lipid vehicles, etc. In some embodiments, oligonucleotides or compositions are administered or delivered parenterally. In some embodiments, oligonucleotides or compositions are administered or delivered intravenously. In some embodiments, oligonucleotides or compositions are administered or delivered intrathecally. In some embodiments, oligonucleotides or compositions are administered or delivered intravitreally. In some embodiments, oligonucleotides or compositions are administered or delivered subcutaneously.

[01092] Among other things, the present disclosure provides technologies for preventing or treating conditions, disorders or diseases. In some embodiments, the present disclosure provides a method for preventing or treating a condition, disorder or disease, comprising administering or delivering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or composition as described herein. In some embodiments, a condition, disorder or disease is amenable to (e.g., can benefit from)

A to I conversion. In some embodiments, the base sequence of the oligonucleotide or oligonucleotides in the oligonucleotide composition is substantially complementary to that of the target nucleic acid comprising a target adenosine. In some embodiments, cells, tissues or organs associated with the condition, disorder or disease comprise or express an ADAR protein. In some embodiments, cells, tissues or organs associated with the condition, disorder or disease comprise or express ADAR1 (e.g., a p110 and/or a p150 forms). In some embodiments, cells, tissues or organs associated with the condition, disorder or disease comprise or express ADAR2. In some embodiments, a condition, disorder or disease is as described herein. In some embodiments, a method comprises converting a target adenosine to I.

[01093] In some embodiments, a subject is administered an oligonucleotide or a composition thereof and an additional agent and/or method, e.g., an additional therapeutic agent and/or method. In some embodiments, an oligonucleotide or composition thereof can be administered alone or in combination with one or more additional therapeutic agents and/or treatment. When administered in combination each component may be administered at the same time or sequentially in any order at different points in time. In some embodiments, each component may be administered separately but sufficiently closely in time so as to provide the desired therapeutic effect. In some embodiments, provided oligonucleotides and additional therapeutic components are administered concurrently. In some embodiments, provided oligonucleotides and additional therapeutic components can be administered as one composition. In some embodiments, at a time point a subject being administered can be exposed to both provided oligonucleotides and additional components at the same time.

[01094] In some embodiments, an additional therapeutic agent can be physically conjugated to an oligonucleotide. In some embodiments, an additional agent is GalNAc. In some embodiments, a provided single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequence can be physically conjugated with an additional agent. In some embodiments, additional agent oligonucleotides can have base sequences, sugars, nucleobases, internucleotidic linkages, patterns of sugar, nucleobase, and/or internucleotidic linkage modifications, patterns of backbone chiral centers, etc., or any combinations thereof, as described in the present disclosure, wherein each T may be independently replaced with U and vice versa. In some embodiments, an oligonucleotide can be physically conjugated to a second oligonucleotide which can decrease (directly or indirectly) the expression, activity, and/or level of a target sequence.

[01095] In some embodiments, a subject can be administered an oligonucleotide and an additional therapeutic agent, wherein the additional therapeutic agent is an agent described herein or known in the art which is useful for treatment of a condition, disorder or disease to be treated.

[01096] In some embodiments, provided single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequence can be co-administered or be used as part of a treatment regimen along with one or more treatment for a condition, disorder or disease or a symptom thereof, including but not limited to: aptamers, lncRNAs, lncRNA inhibitors, antibodies, peptides, small molecules, other oligonucleotides to a target other targets.

[01097] In some embodiments, an additional therapeutic treatment is, as a non-limiting example, a method

of editing a gene

[01098] In some embodiments, an additional therapeutic agent is, as a non-limiting example, an oligonucleotide.

[01099] In some embodiments, a second or additional therapeutic agent can be administered to a subject prior, simultaneously with, or after an oligonucleotide. In some embodiments, a second or additional therapeutic agent can be administered multiple times to a subject, and an oligonucleotide is also administered multiple times to a subject, and the administrations are in any order.

[01100] In some embodiments, an improvement may include decreasing the expression, activity and/or level of a gene or gene product which is too high in a disease state; increasing the expression, activity and/or level of a gene or gene product which is too low in the disease state; and/or decreasing the expression, activity and/or level of a mutant and/or disease-associated variant of a gene or gene product.

[01101] In some embodiments, provided oligonucleotides, e.g., single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequences, can be administered as a pharmaceutical composition, e.g., for treating, ameliorating and/or preventing conditions, disorders or diseases. In some embodiments, provided oligonucleotides comprise at least one chirally controlled internucleotidic linkage. In some embodiments, provided oligonucleotide compositions are chirally controlled.

[01102] Among other things, technologies, e.g., oligonucleotides and compositions thereof, of the present disclosure can provide various improvements and advantages compared to reference technologies (e.g., absence or low levels of chiral control (e.g., stereorandom oligonucleotide compositions (e.g., of oligonucleotides of the same base sequence, or the same constitution, etc.)), and/or absence or low levels of certain modifications and patterns thereof (e.g., 2'-F, non-negatively charged internucleotidic linkages , etc.), such as improved stability, delivery, editing efficiency, pharmacokinetics, and/or pharmacodynamics. In some embodiments, a reference oligonucleotide composition is a stereorandom oligonucleotide composition of oligonucleotides with the same base sequence. In some embodiments, a reference oligonucleotide composition is a stereorandom oligonucleotide composition of oligonucleotides with the same constitution (as appreciated by those skilled in the art, in some embodiments, various salt forms may be properly considered to be of the same constitution). In some embodiments, a reference oligonucleotide is an oligonucleotide comprising no non-negatively charged internucleotidic linkages. In some embodiments, a reference oligonucleotide comprises no n001. In some embodiments, a reference oligonucleotide composition is a composition of oligonucleotides comprising no non-negatively charged internucleotidic linkages. In some embodiments, a reference oligonucleotide composition is a composition of oligonucleotides comprising no n001. In some embodiments, provided technologies may be utilized at lower unit or total doses, and/or may be administered with fewer doses and/or longer dose intervals (e.g., to achieve comparable or better effects) compared to reference technologies. In some embodiments, provided technologies can provide long durability of editing. In some embodiments, provided technologies once administered can provide activities, e.g., target editing, at or above certain levels (e.g., levels useful and/or sufficient to provide certain biological and/or therapeutic

effects) for a period of time, e.g., about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60 or more days, or 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 months, after a last dose. In some embodiments, provided technologies provide low toxicity. In some embodiments, provided technologies may be utilized at higher unit or total doses, and/or may be administered with more doses and/or shorter dose intervals (e.g., to achieve better effects) compared to reference technologies. In some embodiments, a total dose may be administered as a single dose. In some embodiments, a total dose may be administered as two or more single doses. In some embodiments, a total dose administered as a single dose may provide higher maximum editing levels compared to when administered as two or more single doses.

[01103] In some cases, patients who have been administered an oligonucleotide as a medicament may experience certain side effects or adverse effects, including: thrombocytopenia, renal toxicity, glomerulonephritis, and/or coagulation abnormalities; genotoxicity, repeat-dose toxicity of target organs and pathologic effects; dose response and exposure relationships; chronic toxicity; juvenile toxicity; reproductive and developmental toxicity; cardiovascular safety; injection site reactions; cytokine response complement effects; immunogenicity; and/or carcinogenicity. In some embodiments, an additional therapeutic agent is administered to counter-act a side effect or adverse effect of administration of an oligonucleotide. In some embodiments, a particular single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequence can have a reduced capability of eliciting a side effect or adverse effect, compared to a different single-stranded oligonucleotide for site-directed editing of a nucleotide in a target RNA sequence.

[01104] In some embodiments, an additional therapeutic agent can be administered to the patient in order to control or alleviate one or more side effects or adverse effects associated with administration of an oligonucleotide.

[01105] In some embodiments, an oligonucleotide and one or more additional therapeutic agent can be administered to a patient (in any order), wherein the additional therapeutic agent can be administered to the patient in order to control or alleviate one or more side effects or adverse effects associated with administration of the oligonucleotide.

[01106] In some embodiments, an oligonucleotide and one or more additional therapeutic agent can be administered to a patient (in any order), wherein the additional therapeutic agent can be administered to the patient in order to control or alleviate one or more side effects or adverse effects associated with administration of the oligonucleotide.

[01107] In some embodiments, an oligonucleotide and one or more additional therapeutic agent can be administered to a patient (in any order), wherein the additional therapeutic agent can be administered to the patient in order to control or alleviate one or more side effects or adverse effects associated with administration of the oligonucleotide, and wherein the oligonucleotide operates via any biochemical mechanism, including but not limited to: decreasing the level, expression and/or activity of a target gene or a gene product thereof, increasing or decreasing skipping of one or more exons in a target gene mRNA, an ADAR-mediated deamination, a RNaseH-mediated mechanism, a steric hindrance-mediated mechanism, and/or a RNA

interference-mediated mechanism, wherein the oligonucleotide is single- or double-stranded.

[01108] In some embodiments, an oligonucleotide composition and one or more additional therapeutic agent can be administered to a patient (in any order), wherein the additional therapeutic agent can be administered to the patient in order to control or alleviate one or more side effects or adverse effects associated with administration of the oligonucleotide composition, and wherein the oligonucleotide composition can be chirally controlled or comprises at least one chirally controlled internucleotidic linkage (including but not limited to a chirally controlled phosphorothioate).

[01109] In some embodiments, provided technologies can provide editing of two or more sites in a system (e.g., a cell, tissue, organ, animal, etc.) ("multiplex editing"). In some embodiments, provided technologies can target and provide editing of two or more sites of the same transcripts. In some embodiments, provided technologies can target and provide editing of two or more different transcripts, either from the same nucleic acid or different nucleic acids. In some embodiments, provided technologies can target and provide editing of transcripts from two or more different nucleic acids. In some embodiments, provided technologies can target and provide editing of transcripts from two or more different genes. In some embodiments, of the targets simultaneously edited, each is independently at a biologically and/or therapeutically relevant level. In some embodiments, in multiplex editing one or more or all targets are independently edited at a comparable level as editing conducted individually under comparable conditions. In some embodiments, multiplex editing are performed utilizing two or more separate compositions, each of which independently target one or more targets. In some embodiments, compositions are administered concurrently. In some embodiments, compositions are administered with suitable intervals. In some embodiments, one or more compositions are administered prior or subsequently to one or more other compositions. In some embodiments, multiplex editing are performed utilizing a single composition, e.g., a composition comprising two or more pluralities of oligonucleotides, wherein the pluralities target different targets. In some embodiments, each plurality independently targets a different adenosine. In some embodiments, each plurality independently targets a different transcript. In some embodiments, each plurality independently targets a different gene. In some embodiments, two or more pluralities may target the same target, but the pluralities together target the desired targets.

[01110] As described herein, provided technologies can provide a number of advantages. For example, in some embodiments, provided technologies are safer than technologies that act on DNA, as provided technologies can provide RNA edits that are both reversible and tunable (e.g., through adjusting of doses). Additionally and alternatively, as demonstrated herein, provided technologies can provide high levels of editing in systems expressing endogenous ADAR proteins thus avoiding the requirement of introduction of exogenous proteins in various instances. Still further, provided technologies do not require complex oligonucleotides that depend on ancillary delivery vehicles, such as viral vectors or lipid nanoparticles, as utilized in many other technologies, particularly for application beyond cell culture. In some embodiments, provided technologies can provide sequence-specific A-to-I RNA editing with high efficiency using endogenous ADAR enzymes and can be delivered to various systems, e.g., cells, in the absence of artificial

delivery agents.

[01111] Those skilled in the art reading the present disclosure will understand that provided oligonucleotides and compositions thereof may be delivered using a number of technologies in accordance with the present disclosure. In some embodiments, provided oligonucleotides and compositions may be delivered via transfection or lipofection. In some embodiments, provided oligonucleotides and compositions thereof may be delivered in the absence of delivery aids, such as those utilized in transfection or lipofection. In some embodiments, provided oligonucleotides and compositions thereof are delivered with gymnotic delivery. In some embodiments, provided oligonucleotides comprise additional chemical moieties that can facilitate delivery. For example, in some embodiments, additional chemical moieties are or comprise ligand moieties (e.g., *N*-acetylgalactosamine (GalNAc)) for receptors (e.g., asialoglycoprotein receptors). In some embodiments, provided oligonucleotides and compositions thereof can be delivered through GalNAc-mediated delivery. In some embodiments, provided technologies are delivered selectively to target cell populations, locations, tissues, organs, etc. In some embodiments, oligonucleotides or compositions are delivered through targeted delivery, e.g., using ligand moieties like GalNAc. In some embodiments, delivery is systemic delivery. In some embodiments, delivery is local delivery (e.g., via IT, IVT, etc.). In some embodiments, provided technologies provide advantages including delivery and editing without complex delivery vehicles. For example, in some embodiments, substantial delivery and RNA editing without lipids or ligand moieties (e.g., GalNAc) was observed in multiple tissues following a single subcutaneous dose to mice, including in heart, kidney, lung, spleen, white adipose tissue (WAT), brown adipose tissue (BAT), liver, and various liver associated cells such as CD3+ cells (T-cells and subset of NK cells), EpCAM+ cells (e.g., cholangiocytes in liver), liver sinosoidal endothelial cells (LSEC), macrophages (e.g., Kupfer cells), etc.

[01112] In some embodiments, provided technologies, e.g., methods, dosage regimens, etc., may comprise one or more loading doses. In some embodiments, technologies comprising loading doses may provide one or more desired effects or results faster than without such loading doses, for example, in some embodiments, editing levels may be increased or achieved faster than without loading doses. In some embodiments, a loading dose is the same as a non-loading dose (e.g., a maintenance dose, a dose administered in regimens without loading doses, etc.). In some embodiments, a loading dose contains about the same amount of agents, e.g., oligonucleotides, as a non-loading dose. In some embodiments, a loading dose is different from a non-loading dose. In some embodiments, a loading dose contains a reduced amount of agents, e.g., oligonucleotides, compared to a non-loading dose. In some embodiments, a loading dose contains an increased amount of agents, e.g., oligonucleotides, compared to a non-loading dose. In some embodiments, two or more loading doses are utilized, each of which independently contains about the same amount of, less or more agents compared to a non-loading dose. In some embodiments, each loading dose is about the same. In some embodiments, each loading dose contains about the same amount of agents, e.g., oligonucleotides, as a non-loading dose. In some embodiments, one or more loading doses are different from one or more other loading doses. In some embodiments, one or more or all loading doses independently contains more agents, e.g., oligonucleotides,

compared to a non-loading dose. In some embodiments, one or more or all loading doses independently contains less agents, e.g., oligonucleotides, compared to a non-loading dose. In some embodiments, each non-loading dose is about the same. In some embodiments, technologies without loading doses can provide comparable or about the same effects or results after a period of time, e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more weeks, or 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more months.

[01113] Certain technologies for designing (e.g., sugars, nucleobases, internucleotidic linkages stereochemistry, patterns thereof, etc.), manufacturing, assessing, characterizing, using, etc., of oligonucleotides and oligonucleotide compositions for editing adenosine, e.g., in RNA, are described in WO 2021/071858, US 2023/0220384, WO 2022/099159, US 2024/0026358, and WO2023/201095, the entirety of each of which is incorporated herein by reference.

[01114] Among other things, the present disclosure provides an insight that a PNPLA3 nucleic acid (e.g., DNA, RNA, etc.) may be modified by various technologies in accordance with the present disclosure. For example, those skilled in the art would understand that one or more alternative gene editing methods (e.g., CRISPR technologies (e.g., CRISPR/Cas systems), TALE (transcription activator-like effector) technologies (e.g., TALENs), ZFN (zinc finger nuclease) technologies) may be used to introduce a variation in a PNPLA3 nucleic acid (e.g., DNA sequence (e.g., genomic DNA), RNA sequence, etc.). Certain gene editing methods and technologies are reviewed and described in, e.g., Nemudryi et al. Acta Naturae. 2014;6(3):19-40.; Urnov et al. Nat Rev Genet. 2010;11(9):636-646.; Gaudelli et al. Nature. 2017;551(7681):464-471.; and Adli M. Nat Commun. 2018;9(1):1911. Those skilled in the art appreciate that many technologies, e.g., those described in WO 2015/191693, WO 2018/027078, WO 2018/154387, WO 2018/204493, WO 2018/232382, WO 2018/027078, WO2019/079347, WO 2023/052774, WO 2023/168235, US 2018/0073012, US 2019/0093099, US 2020/0399626, US 2021/0317440, US 2024/0076652, US 11795443, etc., can be utilized to perform gene editing (e.g., editing of a PNPLA3 nucleic acid) in accordance with the present disclosure, the technologies of each of which are independently incorporated herein by reference. In some embodiments, one or more gene editing methods may be used to introduce a variation in a PNPLA3 nucleic acid that results in a M148V amino acid mutation in the encoded amino acid sequence. In some embodiments, one or more gene editing methods may edit a codon corresponding to an amino acid at a position corresponding to position 148 of SEQ ID NO: 2. In some embodiments, one or more gene editing methods may introduce a valine at a position in an amino acid encoded by a PNPLA3 nucleic acid corresponding to position 148 of SEQ ID NO: 2. In some embodiments, a CRISPR-Cas may be used to introduce a variation in a PNPLA3 nucleic acid. In some embodiments, a TALEN may be used to introduce a variation in a PNPLA3 nucleic acid. In some embodiments, a ZFN may be used to introduce a variation in a PNPLA3 nucleic acid.

[01115] In some embodiments, the present disclosure provides a method for delivering a compound, e.g., an oligonucleotide, to a system (e.g., a subject), comprising administering a conjugate of the compound (e.g., the oligonucleotide) comprising a targeting moiety, e.g., an ASPGR ligand (e.g., GalNAc). For example, in some embodiments, the present disclosure provides a method for delivering ADR-0110420, comprising

administering ADR-0110420-B. In some embodiments, the present disclosure provides a method for delivering ADR-0110652, comprising administering ADR-0110652-B. In some embodiments, the present disclosure provides a method for delivering ADR-0110667, comprising administering ADR-0110667-B. In some embodiments, the present disclosure provides a method for delivering ADR-0110481, comprising administering ADR-0110481-B. In some embodiments, the present disclosure provides a method for delivering ADR-0111148, comprising administering ADR-0111148-B. In some embodiments, the present disclosure provides a method for delivering ADR-0111146, comprising administering ADR-0111146-B. In some embodiments, the present disclosure provides a method for delivering ADR-0111820, comprising administering ADR-0111820-B. In some embodiments, the present disclosure provides a method for delivering ADR-0111776, comprising administering ADR-0111776-B.

[01116] In some embodiments, the present disclosure provides a method for delivering a compound of formula A-1 or a salt thereof, comprising administering a compound of formula B-1 or a salt thereof. In some embodiments, the present disclosure provides a method for delivering a compound of formula A-2 or a salt thereof, comprising administering a compound of formula B-2 or a salt thereof. In some embodiments, the present disclosure provides a method for delivering a compound of formula A-3 or a salt thereof, comprising administering a compound of formula B-3 or a salt thereof. In some embodiments, the present disclosure provides a method for delivering a compound of formula A-4 or a salt thereof, comprising administering a compound of formula B-4 or a salt thereof.

[01117] In some embodiments, oligonucleotides, compositions, and methods described herein can be used for manufacturing a medicament. In some embodiments, oligonucleotides and compositions described herein can be used for manufacturing a medicament for a method of increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof. In some embodiments, oligonucleotides and compositions described herein can be used for manufacturing a medicament for a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject. In some embodiments, oligonucleotides and compositions described herein can be used for manufacturing a medicament for a method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in PNPLA3 in the genome of a subject susceptible thereto or suffering therefrom. In some embodiments, oligonucleotides and compositions described herein can be used for manufacturing a medicament for preventing or treating a condition, disorder or disease, comprising administering or delivering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or composition described herein. In some embodiments, oligonucleotides and compositions described herein can be used for manufacturing a medicament for modulating a protein interaction with an agent in a system wherein a protein is translated from its encoding RNA, comprising administering to the system an oligonucleotide or composition described herein, wherein an adenosine in the encoding RNA is edited, wherein a protein is translated from the edited mRNA ("the edited protein"), wherein the edited protein differs from the unedited protein at an amino acid residue involving in the protein-agent interaction.

[01118] In some embodiments, the present disclosure provides an oligonucleotide and its stereoisomer including diastereomers. In some embodiments, an oligonucleotide is a diastereomer of an oligonucleotide disclosed herein. In some embodiments, an oligonucleotide is a diastereomer of an oligonucleotide with respect to a chiral linkage phosphorous. In some embodiments, an oligonucleotide is a diastereomer of an oligonucleotide with respect to a PN chiral linkage phosphorous. In some embodiments, an oligonucleotide is a diastereomer of an oligonucleotide with respect to a PS chiral linkage phosphorous. In some embodiments, a diastereomer differs from an oligonucleotide only at chiral linkage phosphorous. In some embodiments, a diastereomer differs from an oligonucleotide only at a single chiral linkage phosphorous. In some embodiments, a composition, e.g., a preparation, of an oligonucleotide comprises the oligonucleotide and a diastereomer thereof.

[01119] The present disclosure incorporates various information, including patent application publications, patents and non-patent references, by reference; in the case of any conflict, the present disclosure will control.

[01120] Among other things, the present disclosure provides the following Embodiments:

1. A nucleic acid comprising a sequence of GCUUCIUSCCUUUCUAC, wherein:
   S is either G or C; and
   each U can be optionally and independently replaced with T.
2. A nucleic acid comprising a sequence with about or at least about 50% sequence identity to GCUUCGUGCCUUUCUACAGUGGCCUUAUCC, wherein each U can be optionally and independently replaced with T.
3. A nucleic acid comprising a sequence with at least 50% sequence identity to GCUUCGUCCCCUUCUACAGUGGCCUUAUCC, wherein each U can be optionally and independently replaced with T.
4. The nucleic acid of any one of the preceding Embodiments, wherein the sequence is codon optimized for expression in a cell.
5. The nucleic acid of any one of the preceding Embodiments, wherein the nucleic acid encodes VDALVCSCFVPF.
6. The nucleic acid of Embodiment 4, wherein the cell is a mammalian cell.
7. The nucleic acid of Embodiment 6, wherein the cell is a human cell.
8. A polypeptide comprising an amino acid sequence with about or at least about 50% sequence identity to VDALVCSCFVPF.
9. A polypeptide comprising an amino acid sequence with about or at least about 50% sequence homology to VDALVCSCFVPF.
10. A polypeptide comprising SEQ ID NO: 2 or a characteristic portion thereof:
MYDAERGWSLSFAGCGFLGFYHVGATRCLSEHAPHLLRDARMLFGASAGALHCVGVLSGIPLEQT
LQVLSDLVRKARSRNIGIFHPSFNLSKFLRQGLCKCLPANVHQLISGKIGISLTRVSDGENVLVSDFRS
KDEVVDALVCSCFVPFYSGLIPPSFRGVRYVDGGVSDNVPFIDAKTTITVSPFYGEYDICPKVKSTNF

LHVDITKLSLRLCTGNLYLLSRAFVPPDLKVLGEICLRGYLDAFRFLEEKGICNRPQPGLKSSSEGMD PEVAMPSWANMSLDSSPESAALAVRLEGDELLDHLRLSILPWDESILDTLSPRLATALSEEMKDKGG YMSKICNLLPIRIMSYVMLPCTLPVESAIAIVQRLVTWLPDMPDDVLWLQWVTSQVFTRVLMCLLP ASRSQMPVSSQQASPCTPEQDWPCWTPCSPKGCPAETKAEATPRSILRSSLNFFLGNKVPAGAEGLS TFPSFSLEKSL (SEQ ID NO: 2).

11. The polypeptide of any one of Embodiments 8-10, comprising a valine at a position that is or corresponds to position 148 of SEQ ID NO: 2.

12. The polypeptide of Embodiment 10, wherein the characteristic portion comprises a valine at a position that is or corresponds to position 148 of SEQ ID NO: 2

13. A polypeptide, comprising a characteristic portion of SEQ ID NO: 2, wherein the characteristic portion comprises V148.

14. A cell comprising the nucleic acid of any one of Embodiments 1-7.

15. A cell comprising or expressing the polypeptide of any one of Embodiments 7-13.

16. A cell comprising the nucleic acid sequence of Embodiment 2 and the nucleic acid sequence of Embodiment 3.

17. The cell of any one of Embodiments 14-16, wherein the cell further comprises a nucleic acid comprising a sequence of GCTTCATGCCTTTCTACAGTGGCCTTATCC.

18. The cell of any one of Embodiments 14-17, wherein the cell further comprises a nucleic acid comprising a sequence of GCTTCATCCCCTTCTACAGTGGCCTTATCC.

19. The cell of any one of Embodiments 14-16, wherein the cell further comprises a polypeptide comprising a I148M variation.

20. The cell of Embodiment 19, wherein the polypeptide comprises an amino acid sequence of VDALVCSCFMPF.

21. The cell of any one of Embodiments 14-20, wherein the cell is a human cell.

22. A method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof, comprising modifying an amino acid residue at a position that is or corresponds to position 148 of SEQ ID NO:2.

23. The method of Embodiment 22, wherein the amino acid is a methionine.

24. The method of Embodiment 22, wherein the amino acid is isoleucine.

25. The method of any one of Embodiments 22-24, wherein the amino acid is modified to be a valine.

26. The method of Embodiment 22, wherein the increased lipase activity is about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 fold of that without the modification.

27. The method of Embodiment 22, wherein the lipase activity is increased as compared that of a PNPLA3 polypeptide comprising M148.

28. The method of Embodiment 22, wherein the lipase activity is comparable to that of a PNPLA3 polypeptide comprising I148.

29. An oligonucleotide capable of editing a target adenosine in a nucleic acid encoding a PNPLA3 polypeptide to produce a PNPLA3 polypeptide variant that differs by at least one amino acid residue.

30. The oligonucleotide of Embodiment 29, wherein the target adenosine is at a position within the nucleic acid corresponding to a codon encoding for an amino acid at position 148 of SEQ ID NO: 1 or 2.

31. The oligonucleotide of Embodiment 30, wherein the amino acid at position 148 is methionine.

32. The oligonucleotide of Embodiment 30, wherein the amino acid at position 148 is isoleucine.

33. An oligonucleotide capable of hybridizing to a target sequence comprising GCUUCAUSCCUUUCUAC, wherein S is either G or C.

34. The oligonucleotide of Embodiment 33, wherein S is G.

35. The oligonucleotide of Embodiment 33, wherein S is C.

36. The oligonucleotide of any one of Embodiments 29-35, wherein the target sequence is in a PNPLA3 transcript.

37. An oligonucleotide, wherein the base sequence of the oligonucleotide comprises at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is identical with or complementary to a base sequence of a PNPLA3 gene or a transcript thereof, wherein the oligonucleotide comprises one or more modified sugars, one or more modified nucleobases, and/or one or more modified internucleotidic linkages.

38. The oligonucleotide of Embodiment 37, wherein the base sequence of the oligonucleotide sequence comprises at least 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is complementary to a PNPLA3 transcript.

39. The oligonucleotide of Embodiment 37, wherein the base sequence of the oligonucleotide sequence comprises at least 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is complementary to a PNPLA3 mRNA.

40. The oligonucleotide of any one of the preceding Embodiments, wherein the base sequence of the oligonucleotide comprises at least 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 contiguous bases of GGAUAAGGCCACUGUAGAAGGGGAUGAAGC, GGGACACGGUGAUGGAGAAGGGCAUGAAGC, AUAAGGCCACUGUAGAAGGGGAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGGAUGAAGC, AGGGAUAAGGCCACUAGAAGGGGAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGGAUGAAGC, GGAUAAGGCCACUGUAGAAGGGCAUGAAGC, GAUAAGGCCACUGUAGAAGGGCAUGAAGCA, AUAAGGCCACUGUAGAAGGGCAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGCAUGAAGC, AGGGAUAAGGCCACUAGAAGGGCAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCAUGAAGC, GAUAAGGCCACUGUAGAAAGGCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, AUAAGGCCACUGUAGAAAGGCAUGAAGCAG, UAAGGCCACUGUAGAAAGGCAUGAAGCAGG, AAGGCCACUGUAGAAAGGCAUGAAGCAGGA,

GGAUAAGGCCACUGUAGAAAGCCAUGAAGC, GGAUAAGGCCACUGUAGAAACGCAUGAAGC, GGAUAAGGCCACUGUAGAAUGGCAUGAAGC, GGAUAAGGCCACUGUAGAUAGGCAUGAAGC, GGAUAAGGCCACUGUAGUAAGGCAUGAAGC, GGAUAAGGCCACUGUACAAAGGCAUGAAGC, GGAUAAGGCCACUGUUGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCGUGAAGC, GGAUAAGGCCACUGUAGAGAGGCAUGAAGC, GGAUAAGGCCACUGUAGGAAGGCAUGAAGC, GGAUAAGGCCACUGUGGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGGGAGGCAUGAAGC, GGAUAAGGCCACUGUGGGGAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGUAUGAAGC, GGAUAAGGCCACUGUAGAAGGGUAUGAAGC, GGAUAAGGCCACUGUGGAAAGGUAUGAAGC, GGGAUAAGGCCACUGUAGAAAGGCAUGAAGCA, or GGAUAAGGCCACUGUAGAAAGGCAUGAAGCAG, wherein each T can be independently replaced with U and vice versa.

41. An oligonucleotide comprising 5'-$N_1N_0N_{-1}$-3', wherein N_1, N_0, and N_{-1} are each independently a nucleoside and are linked by internucleotidic linkages, wherein the oligonucleotide is capable of binding to a target nucleic acid with N_0 opposite to a target adenosine.

42. An oligonucleotide comprising:

a first domain; and

a second domain,

wherein:

the first domain comprises one or more 2'-F modifications;

the second domain comprises one or more sugars that do not have a 2'-F modification.

43. An oligonucleotide comprising a modified nucleobase, nucleoside, sugar or internucleotidic linkage as described in the present disclosure.

44. An oligonucleotide, wherein about or at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% of all sugars are 2'-F modified sugars.

45. An oligonucleotide comprising a second subdomain as described in the present disclosure.

46. An oligonucleotide comprising one or more modified sugars and/or one or more modified internucleotidic linkages, wherein the oligonucleotide comprises a first domain and a second domain each independently comprising one or more nucleobases.

47. The oligonucleotide of any one of Embodiments 29-46, wherein when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, a target adenosine in the target PNPLA3 transcript is modified.

48. The oligonucleotide of any one of Embodiments 29-46, wherein when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of the target PNPLA3 transcript is reduced compared to absence of the product or presence of a reference oligonucleotide.

49. The oligonucleotide of any one of Embodiments 29-46, wherein when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of a product of

the target PNPLA3 transcript is altered compared to absence of the product or presence of a reference oligonucleotide.

50. The oligonucleotide of any one of Embodiments 48-49, wherein the target PNPLA3 transcript is modified.

51. The oligonucleotide of any one of Embodiments 47-50, wherein level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is modified.

52. The oligonucleotide of any one of Embodiments 47-50, wherein level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is replaced with inosine.

53. The oligonucleotide of any one of Embodiments 47-50, wherein level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the adenine of the target adenosine is replaced with guanine.

54. The oligonucleotide of any one of Embodiments 51-53, wherein the product is a protein.

55. The oligonucleotide of Embodiment 54, wherein the product is a PNPLA3 protein.

56. The oligonucleotide of any one of the preceding Embodiments, wherein the target adenosine is more associated with a condition, disorder or disease than a guanine at the same position.

57. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is capable of forming a double-stranded complex with the target PNPLA3 transcript.

58. The oligonucleotide of Embodiment 47-57, wherein a target PNPLA3 transcript or a portion thereof is or comprises RNA.

59. The oligonucleotide of any one of Embodiments 47-58, wherein the target adenosine is of an RNA.

60. The oligonucleotide of any one of Embodiments 47-57, wherein the target adenosine is modified, and the modification is or comprises deamination of the target adenosine.

61. The oligonucleotide of any one of Embodiments 47-60, wherein the target adenosine is modified and the modification is or comprises conversion of the target adenosine to an inosine.

62. The oligonucleotide of any one of Embodiments 47-61, wherein the modification is promoted by an ADAR protein.

63. The oligonucleotide of any one of Embodiments 47-62, wherein the system is an *in vitro* or *ex vivo* system comprising an ADAR protein.

64. The oligonucleotide of any one of Embodiments 47-62, wherein the system is or comprises a cell that comprises or expresses an ADAR protein.

65. The oligonucleotide of any one of Embodiments 47-62, wherein the system is a subject comprising a cell that comprises or expresses an ADAR protein.

66. The oligonucleotide of any one of Embodiments 62-65, wherein the ADAR protein is ADAR1.

67. The oligonucleotide of any one of Embodiments 62-65, wherein the ADAR protein is ADAR2.

68. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 10-200 (e.g., about 10-20, 10-30, 10-40, 10-50, 10-60, 10-70, 10-80, 10-90, 10-100, 10-120, 10-150, 20-30, 20-40, 20-50, 20-60, 20-70, 20-80, 20-90, 20-100, 20-120, 20-150, 20-200, 25-30, 25-40, 25-50, 25-60, 25-70, 25-80, 25-90, 25-100, 25-120, 25-150, 25-200, 30-40, 30-50, 30-60, 30-70, 30-80, 30-90, 30-100, 30-120, 30-150, 30-200, 10, 20, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 60, etc.) nucleobases.

69. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 26-35 nucleobases.

70. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 26 nucleobases.

71. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 27 nucleobases.

72. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 28 nucleobases.

73. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 29 nucleobases.

74. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 30 nucleobases.

75. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 31 nucleobases.

76. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 32 nucleobases.

77. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 33 nucleobases.

78. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 34 nucleobases.

79. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a length of about 35 nucleobases.

80. The oligonucleotide of any one of Embodiments 29-68, wherein the base sequence of the oligonucleotide is complementary to a base sequence of a portion of a target PNPLA3 transcript comprising the target adenosine with 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches which are not Watson-Crick base pairs.

81. The oligonucleotide of Embodiment 80, wherein one or more mismatches are independently a wobble base paring.

82. The oligonucleotide of any one of Embodiments 80-81, wherein the complementarity is about 50%-

100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.).

83. The oligonucleotide of any one of Embodiments 80-81, wherein the complementarity is about 90%-100% or about 95-100%.

84. The oligonucleotide of any one of Embodiments 80-81, wherein the complementarity is 100%.

85. The oligonucleotide of any one of Embodiments 80-81, wherein the complementarity is 100% except at a nucleoside opposite to a target nucleoside (e.g., adenosine).

86. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide can hybridize to a PNPLA3 transcript, wherein the portion the oligonucleotide hybridizes to comprises a target adenosine.

87. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide can hybridize to a PNPLA3 transcript, wherein the portion the oligonucleotide hybridizes to is, comprises, overlaps with, or is gcuucaucccccuucuacaguggccuuaucc or gcuucaugccuuucuacaguggccuuaucc.

88. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine is comparable to or higher than a reference oligonucleotide.

89. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 20% as compared to absence of the oligonucleotide.

90. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 30% as compared to absence of the oligonucleotide.

91. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 40% as compared to absence of the oligonucleotide.

92. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 50% as compared to absence of the oligonucleotide.

93. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 60% as compared to absence of the oligonucleotide.

94. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 1.2-fold greater than a reference

oligonucleotide.

95. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 1.5-fold greater than a reference oligonucleotide.

96. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 2-fold greater than a reference oligonucleotide.

97. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 3-fold greater than a reference oligonucleotide.

98. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 4-fold greater than a reference oligonucleotide.

99. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine at least about 5-fold greater than a reference oligonucleotide.

100. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine is about or at least about 50%, 60%, 70%, 80%, 90%, 100%, 110%, 120%, 130%, 140%, 150%, 160%, 170%, 180%, 190%, or 200% of that of a reference oligonucleotide.

101. The oligonucleotide of any one of the preceding Embodiments, wherein when the oligonucleotide is administered into a system, editing of the target adenosine is about or at least about 100% of that of a reference oligonucleotide.

102. The oligonucleotide of any one of the preceding Embodiments, wherein the reference oligonucleotide is ADR-0108273.

103. The oligonucleotides of any one of the preceding Embodiments, wherein among the first 3, 4, 5, 6, 7, 8, 9, 10 or more sugars from the 5'-end of the oligonucleotide, about one or no more than about 1, 2, 3, or 4 sugars comprises a 2'-F modified sugar.

104. The oligonucleotides of any one of the preceding Embodiments, wherein among the first 6 sugars from the 5'-end of the oligonucleotide, about one or no more than about 1, 2, or 3 sugars comprises a 2'-F modified sugar.

105. The oligonucleotides of any one of the preceding Embodiments, wherein among the first 7 sugars from the 5'-end of the oligonucleotide, about one or no more than about 1, 2, or 3 sugars comprises a 2'-F modified sugar.

106. The oligonucleotide of any one of the preceding Embodiments, wherein the first 3, 4, 5, 6, 7, 8, 9, 10 or more sugars from the 5'-end of the oligonucleotide independently comprise a 2'-OR modification,

wherein R is optionally substituted C_{1-6} aliphatic.

107. The oligonucleotide of Embodiment 105, wherein in each 2'-OR modification, R is independently optionally substituted C_{1-6} aliphatic.

108. The oligonucleotide of Embodiment 105, wherein each 2'-OR modification is independently a 2'-OMe or a 2'-MOE modification.

109. The oligonucleotide of Embodiment 105, wherein each 2'-OR modification is independently a 2'-OMe modification.

110. The oligonucleotide of any one of the preceding Embodiments, wherein the percentage of 2'-F modified sugars for all sugars at the 5' side of N_0 is about or at least about 40%, 50%, 60%, 70%, 80%, or 90%.

111. The oligonucleotide of Embodiment 111, wherein the percentage is about or at least about 50%.

112. The oligonucleotide of any one of the preceding Embodiments, wherein the percentage of 2'-OR modified sugars for all sugars at the 5' side of N_0 is about or at least 20%, 30%, 40%, 50%, or 60%, wherein each R is optionally substituted C_{1-6} aliphatic.

113. The oligonucleotide of any one of the preceding Embodiments, wherein the percentage of 2'-OMe modified sugars for all sugars at the 5' side of N_0 is about or at least about 20%, 30%, 40%, 50%, or 60%.

114. The oligonucleotide of any one of Embodiments 112-113, wherein the percentage is about or no more than about 50%.

115. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{24} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

116. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the first nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

117. The oligonucleotide of any one of Embodiments 115-116, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

118. The oligonucleotide of any one of Embodiments 115-116, wherein the 2'-OR modified sugar is a 2'-MOE modified sugar.

119. The oligonucleotide of any one of Embodiments 1-114, wherein the sugar of N_{24} is m1d.

120. The oligonucleotide of any one of Embodiments 1-114, wherein the sugar of the first nucleoside from the 5'-end of the oligonucleotide is m1d.

121. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{23} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

122. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the second nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

123. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{22} is a 2'-OR

modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

124. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the third nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

125. The oligonucleotide of any one of Embodiments 120-124, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

126. The oligonucleotide of any one of Embodiments 120-124, wherein the 2'-OR modified sugar is a 2'-MOE modified sugar.

127. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{20} is a 2'-F modified sugar.

128. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 5th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

129. The oligonucleotide of any one of Embodiments 1-126, wherein the sugar of N_{20} is 2'-deoxyribose (DNA sugar).

130. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{12} is a DNA sugar.

131. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{13} is a DNA sugar.

132. The oligonucleotide of any one of Embodiments 1-126, wherein the sugar of the 5th nucleoside from the 5'-end of the oligonucleotide is 2'-deoxyribose (DNA sugar).

133. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{19} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

134. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 6th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

135. The oligonucleotide of any one of Embodiments 133-134, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

136. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{17} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

137. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 8th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

138. The oligonucleotide of any one of Embodiments 136-137, the 2'-OR modified sugar is a 2'-MOE modified sugar.

139. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{16} is a 2'-F modified sugar.

140. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 9th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

141. The oligonucleotide of any one of Embodiments 1-138, wherein the sugar of N_{16} is m1d.

142. The oligonucleotide of any one of Embodiments 1-138, wherein the sugar of the 9th nucleoside from the 5'-end of the oligonucleotide is m1d.

143. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{15} is a 2'-F modified sugar.

144. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 10th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

145. The oligonucleotide of any one of Embodiments 1-142, wherein the sugar of N_{15} is m1d.

146. The oligonucleotide of any one of Embodiments 1-142, wherein the sugar of the 10th nucleoside from the 5'-end of the oligonucleotide is m1d.

147. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{13} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

148. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 12th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

149. The oligonucleotide of any one of Embodiments 147-148, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

150. The oligonucleotide of any one of Embodiments 1-146, wherein the sugar of N_{13} is a 2'-F modified sugar.

151. The oligonucleotide of any one of Embodiments 1-146, wherein the sugar of the 12th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

152. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{12} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

153. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 13th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

154. The oligonucleotide of any one of Embodiments 152-153, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

155. The oligonucleotide of Embodiments 1-151, wherein the sugar of N_{12} is a 2'-F modified sugar.

156. The oligonucleotide of Embodiments 1-151, wherein the sugar of the 13th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

157. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{11} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

158. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 14th

nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

159. The oligonucleotide of any one of Embodiments 157-158, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

160. The oligonucleotide of Embodiments 1-156, wherein the sugar of N_{11} is a 2'-F modified sugar.

161. The oligonucleotide of Embodiments 1-156, wherein the sugar of the 14th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

162. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_9 is a 2'-F modified sugar.

163. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 16th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

164. The oligonucleotide of any one of Embodiments 1-161, wherein the sugar of N_9 is m1d.

165. The oligonucleotide of any one of Embodiments 1-161, wherein the sugar of the 16th nucleoside from the 5'-end of the oligonucleotide is m1d.

166. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_8 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

167. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 17th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

168. The oligonucleotide of any one of Embodiments 166-167, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

169. The oligonucleotide of Embodiments 1-165, wherein the sugar of N_8 is a 2'-F modified sugar.

170. The oligonucleotide of Embodiments 1-165, wherein the sugar of the 17th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

171. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_7 is a 2'-F modified sugar.

172. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 18th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

173. The oligonucleotide of any one of Embodiments 1-170, wherein the sugar of N_7 is m1d.

174. The oligonucleotide of any one of Embodiments 1-170, wherein the sugar of the 18th nucleoside from the 5'-end of the oligonucleotide is m1d.

175. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_6 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

176. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 19th nucleoside from the 5'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

177. The oligonucleotide of any one of Embodiments 175-176, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

178. The oligonucleotide of Embodiments 1-174, wherein the sugar of N_6 is a 2'-F modified sugar.

179. The oligonucleotide of Embodiments 1-174, wherein the sugar of the 19th nucleoside from the 5'-end of the oligonucleotide is a 2'-F modified sugar.

180. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_1 is a deoxyribose.

181. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_0 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

182. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_0 is a 2'-OMe modified sugar.

183. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_0 is a deoxyribose.

184. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-1} is a deoxyribose.

185. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-2} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

186. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-2} is a 2'-OMe modified sugar.

187. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-3} is a 2'-F modified sugar.

188. The oligonucleotide of any one of Embodiments 1-186, wherein the sugar of N_{-3} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

189. The oligonucleotide of any one of Embodiments 1-186, wherein the sugar of N_{-3} is a 2'-Me modified sugar.

190. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-4} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

191. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-4} is a 2'-OMe modified sugar.

192. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 2nd nucleoside from the 3'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

193. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 2nd nucleoside from the 3'-end of the oligonucleotide is a 2'-OMe modified sugar.

194. The oligonucleotide of any one of Embodiments 1-189, wherein the sugar of N_{-4} is a bicyclic sugar.

195. The oligonucleotide of any one of Embodiments 1-189, wherein the sugar of N_{-4} is a LNA sugar.

196. The oligonucleotide of any one of Embodiments 1-189, wherein the sugar of the 2nd nucleoside from the 3'-end of the oligonucleotide is a bicyclic sugar.

197. The oligonucleotide of any one of Embodiments 1-189, wherein the sugar of the 2nd nucleoside from the 3'-end of the oligonucleotide is a LNA sugar.

198. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-5} is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

199. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-5} is a 2'-OMe modified sugar.

200. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 1st nucleoside from the 3'-end of the oligonucleotide is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

201. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of the 1st nucleoside from the 3'-end of the oligonucleotide is a 2'-OMe modified sugar.

202. The oligonucleotide of any one of Embodiments 1-197, wherein the sugar of N_{-5} is a bicyclic sugar.

203. The oligonucleotide of any one of Embodiments 1-197, wherein the sugar of N_{-5} is a LNA sugar.

204. The oligonucleotide of any one of Embodiments 1-197, wherein the sugar of the 1st nucleoside from the 3'-end of the oligonucleotide is a bicyclic sugar.

205. The oligonucleotide of any one of Embodiments 1-197, wherein the sugar of the 1st nucleoside from the 3'-end of the oligonucleotide is a LNA sugar.

206. The oligonucleotide of any one of Embodiments 115-205, wherein the 2'-OR modified sugar is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} alkyl.

207. The oligonucleotide of any one of Embodiments 115-205, wherein the 2'-OR modified sugar is a 2'-OMe or 2'-MOE modified sugar.

208. The oligonucleotide of any one of the preceding Embodiments, wherein each sugar of N_2, N_3, N_4, N_5, N_7, N_9, N_{10}, N_{14}, N_{15}, N_{16}, N_{18} and N_{21} is independently a 2'-F modified sugar.

209. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{23} and N_{22} is a natural phosphate linkage.

210. The oligonucleotide of any one of the preceding Embodiments, wherein the 2nd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

211. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{22} and N_{21} is a natural phosphate linkage.

212. The oligonucleotide of any one of the preceding Embodiments, wherein the 3rd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

213. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{17} and N_{16} is a natural phosphate linkage.

214. The oligonucleotide of any one of the preceding Embodiments, wherein the 8th internucleotidic

linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

215. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{11} and N_{10} is a natural phosphate linkage.

216. The oligonucleotide of any one of the preceding Embodiments, wherein the 14th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

217. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage.

218. The oligonucleotide of any one of the preceding Embodiments, wherein the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

219. The oligonucleotide of any one of Embodiments 1-216, wherein the internucleotidic linkage between N_8 and N_7 is a phosphorothioate internucleotidic linkage.

220. The oligonucleotide of any one of Embodiments 1-216, wherein the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a phosphorothioate internucleotidic linkage.

221. The oligonucleotide of any one of Embodiments 1-216, wherein the internucleotidic linkage between N_8 and N_7 is a *Sp* phosphorothioate internucleotidic linkage.

222. The oligonucleotide of any one of Embodiments 1-216, wherein the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage.

223. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_6 and N_5 is a natural phosphate linkage.

224. The oligonucleotide of any one of the preceding Embodiments, wherein the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

225. The oligonucleotide of any one of Embodiments 1-222, wherein the internucleotidic linkage between N_6 and N_5 is a phosphorothioate internucleotidic linkage.

226. The oligonucleotide of any one of Embodiments 1-222, wherein the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a phosphorothioate internucleotidic linkage.

227. The oligonucleotide of any one of Embodiments 1-222, wherein the internucleotidic linkage between N_6 and N_5 is a *Sp* phosphorothioate internucleotidic linkage.

228. The oligonucleotide of any one of Embodiments 1-222, wherein the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage.

229. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage.

230. The oligonucleotide of any one of the preceding Embodiments, wherein the 27th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

231. The oligonucleotide of any one of Embodiments 209-230, wherein linkage phosphorus of the natural phosphate linkage is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside, wherein the nucleoside comprises a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

232. The oligonucleotide of any one of the preceding Embodiments, wherein linkage phosphorus of each natural phosphate linkage is independently bonded to an oxygen atom bonded to the 3'-carbon of a nucleoside, wherein the nucleoside comprises a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

233. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{24} and N_{23} is a PN linkage.

234. The oligonucleotide of any one of the preceding Embodiments, wherein the 1st internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

235. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{13} and N_{12} is a PN linkage.

236. The oligonucleotide of any one of the preceding Embodiments, wherein the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

237. The oligonucleotide of any one of Embodiments 1-234, wherein the internucleotidic linkage between N_{13} and N_{12} is a phosphorothioate internucleotidic linkage.

238. The oligonucleotide of any one of Embodiments 1-234, wherein the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a phosphorothioate internucleotidic linkage.

239. The oligonucleotide of any one of Embodiments 1-234, wherein the internucleotidic linkage between N_{13} and N_{12} is a *Sp* phosphorothioate internucleotidic linkage.

240. The oligonucleotide of any one of Embodiments 1-234, wherein the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage.

241. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{12} and N_{11} is a PN linkage.

242. The oligonucleotide of any one of Embodiments 1-236, wherein the internucleotidic linkage between N_{13} and N_{12} is a PN linkage and the internucleotidic linkage between N_{12} and N_{11} is a PN linkage.

243. The oligonucleotide of any one of the preceding Embodiments, wherein the 13th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

244. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_9 and N_8 is a PN linkage.

245. The oligonucleotide of any one of the preceding Embodiments, wherein the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

246. The oligonucleotide of any one of Embodiments 1-243, wherein the internucleotidic linkage between N_9 and N_8 is a phosphorothioate internucleotidic linkage.

247. The oligonucleotide of any one of Embodiments 1-243, wherein the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a phosphorothioate internucleotidic linkage.

248. The oligonucleotide of any one of Embodiments 1-243, wherein the internucleotidic linkage between N_9 and N_8 is a *Sp* phosphorothioate internucleotidic linkage.

249. The oligonucleotide of any one of Embodiments 1-243, wherein the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a *Sp* phosphorothioate internucleotidic linkage.

250. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a PN linkage.

251. The oligonucleotide of any one of the preceding Embodiments, wherein the 26th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

252. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a PN linkage.

253. The oligonucleotide of any one of the preceding Embodiments, wherein the 29th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

254. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN internucleotidic linkage.

255. The oligonucleotide of any one of the preceding Embodiments, wherein the PN internucleotidic linkage is a phosphoramidate internucleotidic linkage.

256. The oligonucleotide of any one of the preceding Embodiments, wherein the PN internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage.

257. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is n001.

258. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is n006.

259. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is n025.

260. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is MsPA.

261. The oligonucleotide of any one of the preceding Embodiments, wherein the linkage phosphorus of the PN internucleotidic linkage is *Rp*.

262. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is *Rp* n001.

263. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is *Rp* n006.

264. The oligonucleotide of any one of Embodiments 233-254, wherein the PN internucleotidic linkage is *Rp* n025.

265. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently a natural phosphate linkage, a phosphorothioate internucleotidic linkage, or a PN internucleotidic linkage.

266. The oligonucleotide of any one of the preceding Embodiments, wherein each phosphorothioate

internucleotidic linkage is independently *Sp*.

267. The oligonucleotide of any one of the preceding Embodiments, wherein each PN internucleotidic linkage is independently a phosphoramidate internucleotidic linkage.

268. The oligonucleotide of any one of the preceding Embodiments, wherein each PN internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage or MsPA.

269. The oligonucleotide of any one of Embodiments 1-259 and 261-268, wherein each PN internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage.

270. The oligonucleotide of any one of Embodiments 1-257, 260-262 and 265-269, wherein each PN internucleotidic linkage is independently n001.

271. The oligonucleotide of any one of Embodiments 1-257, 260-262 and 265-269, wherein each PN internucleotidic linkage is independently n006.

272. The oligonucleotide of any one of the preceding Embodiments, wherein N_4 produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

273. The oligonucleotide of any one of the preceding Embodiments, wherein N_4 produces a C-C mismatch base pairing aligned with a target nucleic acid.

274. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of N_4 is C.

275. The oligonucleotide of any one of the preceding Embodiments, wherein the 21st nucleoside from the 5'-end of the oligonucleotide produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

276. The oligonucleotide of any one of the preceding Embodiments, wherein the 21st nucleoside from the 5'-end of the oligonucleotide produces a C-C mismatch base pairing aligned with a target nucleic acid.

277. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of the 21st nucleoside from the 5'-end of the oligonucleotide is C.

278. The oligonucleotide of any one of Embodiments 1-270, wherein the nucleobase of N_4 is G.

279. The oligonucleotide of any one of Embodiments 1-270, wherein the nucleobase of the 21st nucleoside from the 5'-end of the oligonucleotide is G.

280. The oligonucleotide of any one of the preceding Embodiments, wherein N_9 produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

281. The oligonucleotide of any one of the preceding Embodiments, wherein N_9 produces a G-U wobble base pairing aligned with a target nucleic acid.

282. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of N_9 is G.

283. The oligonucleotide of any one of the preceding Embodiments, wherein the 16th nucleoside from the 5'-end of the oligonucleotide produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

284. The oligonucleotide of any one of the preceding Embodiments, wherein the 16th nucleoside from the 5'-end of the oligonucleotide produces a G-U wobble base pairing aligned with a target nucleic acid.

285. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of the 16th nucleoside from the 5'-end of the oligonucleotide is G.

286. The oligonucleotide of any one of Embodiments 1-279, wherein the nucleobase of N_9 is A.

287. The oligonucleotide of any one of Embodiments 1-279, wherein the nucleobase of the 16th nucleoside from the 5'-end of the oligonucleotide is A.

288. The oligonucleotide of any one of the preceding Embodiments, wherein N_{20} produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

289. The oligonucleotide of any one of the preceding Embodiments, wherein N_{20} produces a mismatch when the oligonucleotide is aligned with a target nucleic acid.

290. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of N_{20} is T.

291. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of N_{20} is U.

292. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of N_{20} is A.

293. The oligonucleotide of any one of the preceding Embodiments, wherein the 5th nucleoside from the 5'-end of the oligonucleotide produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

294. The oligonucleotide of any one of the preceding Embodiments, wherein the 5th nucleoside from the 5'-end of the oligonucleotide produces a mismatch when the oligonucleotide is aligned with a target nucleic acid.

295. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of the 5th nucleoside from the 5'-end of the oligonucleotide is T.

296. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of the 5th nucleoside from the 5'-end of the oligonucleotide is U.

297. The oligonucleotide of any one of Embodiments 1-287, wherein the nucleobase of the 5th nucleoside from the 5'-end of the oligonucleotide is A.

298. The oligonucleotide of any one of the preceding Embodiments, wherein N_{16} produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

299. The oligonucleotide of any one of the preceding Embodiments, wherein N_{16} produces a G-U wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

300. The oligonucleotide of any one of Embodiments 1-297, wherein the nucleobase of N_{16} is U.

301. The oligonucleotide of any one of the preceding Embodiments, wherein the 9th nucleoside from the 5'-end of the oligonucleotide produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

302. The oligonucleotide of any one of the preceding Embodiments, wherein the 9th nucleoside from the 5'-end of the oligonucleotide produces a G-U wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

303. The oligonucleotide of any one of Embodiments 1-297, wherein the nucleobase of the 9th nucleoside

from the 5'-end of the oligonucleotide is U.

304. The oligonucleotide of any one of the preceding Embodiments, wherein N_{24} is the first nucleoside.

305. The oligonucleotide of any one of the preceding Embodiments, wherein N_{23} is the first nucleoside.

306. The oligonucleotide of any one of Embodiments 29-87, wherein the oligonucleotide consists of a first domain and a second domain.

307. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

308. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain has a length of about 10-25 nucleobases.

309. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target nucleic acid for complementarity.

310. The oligonucleotide of any one of Embodiments 41-307, wherein the first domain is fully complementary to a target nucleic acid.

311. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) sugars with 2'-F modification.

312. The oligonucleotide of any one of the preceding Embodiments, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in the first domain independently comprise a 2'-F modification.

313. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) consecutive sugars with 2'-F modification.

314. The oligonucleotide of any one of the preceding Embodiments, wherein about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain comprises 2'-OMe.

315. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain comprises 2'-OMe.

316. The oligonucleotide of any one of the preceding Embodiments, wherein about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic.

317. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic.

318. The oligonucleotide of any one of the preceding Embodiments, wherein about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain are natural DNA sugars.

319. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain are natural DNA sugars.

320. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

321. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-MOE modification.

322. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification.

323. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises two or more (e.g., about 2-20, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) consecutive modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

324. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises two or more (e.g., about 2-20, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) consecutive modified sugars comprising a 2'-MOE modification.

325. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises two or more (e.g., about 2-20, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) consecutive modified sugars comprising a 2'-OMe modification

326. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) natural

DNA sugars.The oligonucleotide of any one of the preceding Embodiments, wherein the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic.

327. The oligonucleotide of any one of the preceding Embodiments, wherein the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-OMe modified sugar.

328. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-$N(R)_2$ modification, wherein each R is optionally substituted C_{1-6} aliphatic.

329. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) LNA sugars.

330. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

331. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages.

332. The oligonucleotide of any one of the preceding Embodiments, wherein about 50%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in the first domain are modified internucleotidic linkages.

333. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkage is independently a chiral internucleotidic linkage.

334. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a PN or a PS linkage.

335. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage.

336. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage.

337. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or phosphoryl guanidine internucleotidic linkage.

338. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more phosphorothioate internucleotidic linkages.

339. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more PN internucleotidic linkages.

340. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more phosphoryl guanidine internucleotidic linkages.

341. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n001 internucleotidic linkages.

342. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n006 internucleotidic linkages.

343. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n003 internucleotidic linkages.

344. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n008 internucleotidic linkages.

345. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n025 internucleotidic linkages.

346. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n026 internucleotidic linkages.

347. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises one or more n078 internucleotidic linkages.

348. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain comprises 1, 2, 3, 4, or 5 non-negatively charged internucleotidic linkages.

349. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a modified internucleotidic linkage.

350. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a non-negatively charged internucleotidic linkage.

351. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a PN internucleotidic linkage.

352. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a phosphoryl guanidine internucleotidic linkage.

353. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage

between the first and the second nucleosides of the first domain is a n001 internucleotidic linkage.

354. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a n006 internucleotidic linkage.

355. The oligonucleotide of any one of Embodiments 1-349, wherein the modified internucleotidic linkage is a phosphorothioate internucleotidic linkage.

356. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the first domain is a non-negatively charged internucleotidic linkage.

357. The oligonucleotide of any one of the preceding Embodiments, wherein at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in the first domain is chirally controlled.

358. The oligonucleotide of any one of the preceding Embodiments, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in the first domain is chirally controlled.

359. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is chirally controlled.

360. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the first domain is chirally controlled.

361. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral internucleotidic linkage is independently a chirally controlled internucleotidic linkage.

362. The oligonucleotide of any one of the preceding Embodiments, wherein at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in the first domain is Sp.

363. The oligonucleotide of any one of the preceding Embodiments, wherein at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-

100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in the first domain is *Sp*.

364. The oligonucleotide of any one of Embodiments 42-363, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is *Rp*.

365. The oligonucleotide of any one of Embodiments 42-364, wherein the first domain comprises one or more natural phosphate linkages.

366. The oligonucleotide of any one of Embodiments 42-364, wherein the first domain comprises no more than about 5 natural phosphate linkages.

367. The oligonucleotide of any one of the preceding Embodiments, wherein the first domain can interact, or promotes or contributes to interaction of, an ADAR protein with a target nucleic acid.

368. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

369. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain has a length of about 9-25 nucleobases.

370. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain has a length of about 9-15 nucleobases.

371. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target nucleic acid for complementarity.

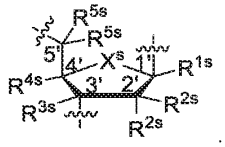
372. The oligonucleotide of any one of the preceding Embodiments, comprising a sugar that comprises a 6-membered ring having 0-2 (0, 1, or 2) heteroatoms.

373. The oligonucleotide of any one of the preceding Embodiments, comprising a bicyclic sugar.

374. The oligonucleotide of any one of the preceding Embodiments, comprising a LNA sugar.

375. The oligonucleotide of any one of the preceding Embodiments, comprising a cEt sugar.

376. The oligonucleotide of any one of the preceding Embodiments, comprising a (S)-cEt sugar.

377. The oligonucleotide of any one of the preceding Embodiments, comprising a sugar that has the structure of 

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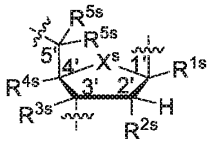
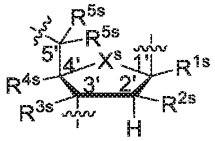
378. The oligonucleotide of Embodiment 377, wherein each R^{2s} is independently −H, −F, −OH or $-OR^{ak}$, wherein R^{ak} is optionally substituted C_{1-6} aliphatic.

379. The oligonucleotide of any one of Embodiments 377-378, wherein the sugar has the structure of



380. The oligonucleotide of any one of Embodiments 377-379, wherein the sugar has the structure of



381. The oligonucleotide of any one of Embodiments 377-380, wherein R^{1s} is −H.

382. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is −H.

383. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is −F.

384. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is −OH.

385. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is $-OR^{ak}$, wherein R^{ak} is optionally substituted C_{1-6} aliphatic.

386. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is −OMe.

387. The oligonucleotide of any one of Embodiments 377-381, wherein R^{2s} is $-OCH_2CH_2OCH_3$.

388. The oligonucleotide of any one of Embodiments 377-387, wherein R^{3s} is −H.

389. The oligonucleotide of any one of Embodiments 377-388, wherein R^{4s} is −H.

390. The oligonucleotide of any one of Embodiments 377-389, wherein one occurrence of R^{5s} is −H.

391. The oligonucleotide of any one of Embodiments 377-390, wherein the other occurrence of R^{5s} is −H.

392. The oligonucleotide of any one of Embodiments 377-390, wherein the other occurrence of R^{5s} is optionally substituted C_{1-6} aliphatic.

393. The oligonucleotide of any one of Embodiments 377-392, wherein X^s is −O−.

394. The oligonucleotide of any one of Embodiments 377-392, wherein X^s is −S−.

395. The oligonucleotide of any one of Embodiments 377-392, wherein X^s is optionally substituted $-CH_2-$.

396. The oligonucleotide of any one of Embodiments 377-392, wherein X^s is $-CH_2-$.

397. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 − about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars with a 2'-F modification.

398. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

399. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification.

400. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-MOE modification.

401. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) LNA sugars.

402. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

403. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) natural DNA sugars.

404. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages.

405. The oligonucleotide of any one of the preceding Embodiments, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in the second domain are modified internucleotidic linkages.

406. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a chiral internucleotidic linkage.

407. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a PN or PS internucleotidic linkage.

408. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage.

409. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral

internucleotidic linkage.

410. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a phosphoryl guanidine internucleotidic linkage.

411. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more phosphorothioate internucleotidic linkages.

412. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more PN internucleotidic linkages.

413. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more phosphoryl guanidine internucleotidic linkages.

414. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more n001 internucleotidic linkages.

415. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises one or more n006 internucleotidic linkages.

416. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises 1, 2, 3, 4, or 5 non-negatively charged internucleotidic linkages.

417. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a modified internucleotidic linkage.

418. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a non-negatively charged internucleotidic linkage.

419. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a PN internucleotidic linkage.

420. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a phosphoryl guanidine internucleotidic linkage.

421. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a n001 internucleotidic linkage.

422. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a n006 internucleotidic linkage.

423. The oligonucleotide of any one of Embodiments 1-417, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is a phosphorothioate internucleotidic linkage.

424. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the second domain is a non-negatively charged internucleotidic linkage.

425. The oligonucleotide of any one of the preceding Embodiments, wherein at least about 1-50 (e.g.,

about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in the second domain is chirally controlled.

426. The oligonucleotide of any one of the preceding Embodiments, wherein at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in the second domain is chirally controlled.

427. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is chirally controlled.

428. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the second domain is a chirally controlled.

429. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral internucleotidic linkage is independently a chirally controlled internucleotidic linkage.

430. The oligonucleotide of any one of the preceding Embodiments, wherein at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in the second domain is *Sp*.

431. The oligonucleotide of any one of the preceding Embodiments, wherein at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in the second domain is *Sp*, or wherein each chiral internucleotidic linkages in the second domain is *Sp*.

432. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the first and the second nucleosides of the second domain is *Rp*.

433. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the second domain is *Rp*.

434. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage in the second domain is independently a modified internucleotidic linkage.

435. The oligonucleotide of any one of Embodiments 42-434, wherein the second domain comprises one or more natural phosphate linkages.

436. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain can recruit, or promotes or contributes to recruitment of, an ADAR protein to a target nucleic acid.

437. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain can interact, or promotes or contributes to interaction of, an ADAR protein with a target nucleic acid.

438. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain contacts with a domain that have an enzymatic activity.

439. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain contact with a domain that has a deaminase activity of ADAR1.

440. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain contact with a domain that has a deaminase activity of ADAR2.

441. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises or consists of from the 5' to 3' a second subdomain, and a third subdomain.

442. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises or consists of from the 5' to 3' a first subdomain, a second subdomain, and a third subdomain.

443. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain consists of from the 5' to 3' a first subdomain, a second subdomain, and a third subdomain.

444. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain has a length of about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

445. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-F modification.

446. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) natural DNA sugars.

447. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

448. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification.

449. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.)

modified sugars comprising a 2'-MOE modification.

450. The oligonucleotide of any one of the preceding Embodiments, wherein the first subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) LNA sugars.

451. The oligonucleotide of any one of the preceding Embodiments, wherein the last nucleoside of the first subdomain comprises a 2'-F modified sugar.

452. The oligonucleotide of any one of the preceding Embodiments, wherein the second subdomain has a length of about 1-10 (e.g., about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10) nucleobases.

453. The oligonucleotide of any one of the preceding Embodiments, wherein the second subdomain has a length of about 1-5 (e.g., about 1, 2, 3, 4, or 5) nucleobases.

454. The oligonucleotide of any one of the preceding Embodiments, wherein the second subdomain has a length of 3 nucleobases.

455. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises a nucleoside N_0 opposite to a target adenosine when the oligonucleotide is aligned with a target nucleic acid for complementarity.

456. The oligonucleotide of any one of the preceding Embodiments, wherein the second domain comprises 5'-$N_1N_0N_{-1}$-3', wherein N_0 is opposite to a target adenosine.

457. The oligonucleotide of any one of the preceding Embodiments, wherein the second subdomain comprises a nucleoside N_0 opposite to a target adenosine when the oligonucleotide is aligned with a target nucleic acid for complementarity.

458. The oligonucleotide of any one of the preceding Embodiments, wherein the second subdomain comprises 5'-$N_1N_0N_{-1}$-3', wherein N_0 is opposite to a target adenosine.

459. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

460. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 5-10 (e.g., 5, 6, 7, 8, 9, or 10) nucleobases.

461. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 5 or more nucleobases.

462. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 6 or more nucleobases.

463. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 7 or more nucleobases.

464. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain has a length of about 8 or more nucleobases.

465. The oligonucleotide of any one of the preceding Embodiments, wherein the length of the third subdomain is shorter than the first domain.

466. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) LNA sugars.

467. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) acyclic sugars (e.g., UNA sugars).

468. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-F modification.

469. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) natural DNA sugars.

470. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

471. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification.

472. The oligonucleotide of any one of the preceding Embodiments, wherein the third subdomain comprise about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages.

473. The oligonucleotide of any one of the preceding Embodiments, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in the third subdomain are modified internucleotidic linkages.

474. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a chiral internucleotidic linkage.

475. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the third subdomain is a non-negatively charged

internucleotidic linkage.

476. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the third subdomain is a PN internucleotidic linkage.

477. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the third subdomain is a phosphoryl guanidine internucleotidic linkage.

478. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the third subdomain is a n001 internucleotidic linkage.

479. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between the last and the second last nucleosides of the third subdomain is a n006 internucleotidic linkage.

480. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a PN or PS internucleotidic linkage.

481. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage.

482. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage.

483. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a PN internucleotidic linkage.

484. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a phosphoryl guanidine internucleotidic linkage.

485. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a n001 internucleotidic linkage.

486. The oligonucleotide of any one of the preceding Embodiments, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a n006 internucleotidic linkage.

487. The oligonucleotide of any one of the preceding Embodiments, wherein at least about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) chiral internucleotidic linkages in the third subdomain is chirally controlled.

488. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral internucleotidic

linkage is independently a chirally controlled internucleotidic linkage.

489. The oligonucleotide of any one of the preceding Embodiments, wherein if any, at least one or each neutral internucleotidic linkage is independently n001.

490. The oligonucleotide of any one of the preceding Embodiments, wherein no more than 5, 6, 7, 8, 9, 10, 11 or 12 nucleosides 3' to a nucleoside opposite to a target adenosine

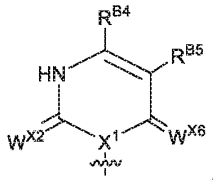
491. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of N_0 is optionally substituted or protected U, C, or A, or is an optionally substituted or protected tautomer of U, C or A.

492. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is hypoxanthine, T, A, G, U, C, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3ne5U], [3nT], [3nfl5U], [3npry5U], [3ncn5U], [napth6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], zndp, or is selected from Table BA-1.

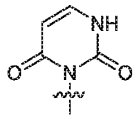
493. The oligonucleotide of any one of Embodiments 1-491, wherein the nucleobase of N_0 is C.

494. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is BA, wherein BA is Ring BA or a tautomer thereof, wherein Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 hetereoatoms.

495. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 has the structure of formula BA-III-e:



496. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is



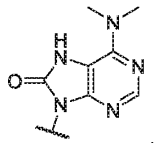
497. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is [o8A].

498. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is [m5C].

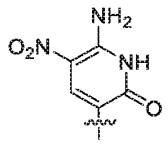
499. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is U.

500. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is T.

501. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is



502. The oligonucleotide of any one of Embodiments 1-490, wherein the nucleobase of N_0 is



503. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_0 is a 2'-F modified sugar.

504. The oligonucleotide of any one of Embodiments 41-502, wherein the sugar of N_0 is a sugar comprising no substituent at a position corresponding to 2'−OH of a natural RNA sugar.

505. The oligonucleotide of any one of Embodiments 41-502, wherein the sugar of N_0 is a sugar comprising no 2'-substituent.

506. The oligonucleotide of any one of Embodiments 41-502, wherein the sugar of N_0 is a modified sugar.

507. The oligonucleotide of any one of Embodiments 41-502, wherein the sugar of N_0 is a 2'-modified sugar.

508. The oligonucleotide of Embodiment 506, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

509. The oligonucleotide of Embodiment 506, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl.

510. The oligonucleotide of Embodiment 506, wherein the modified sugar is a 2'-OMe modified sugar.

511. The oligonucleotide of Embodiment 506, wherein the modified sugar is a 2'-MOE modified sugar.

512. The oligonucleotide of Embodiment 506, wherein the modified sugar is a LNA sugar.

513. The oligonucleotide of any one of Embodiments 41-502, wherein the sugar of N_0 is a natural RNA sugar.

514. The oligonucleotide of any one of the preceding Embodiments, wherein nucleobase of N_1 is A, T, C, G, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [napth6o8A], [ipr6o8A], [c7In], [c39z48In], [z2c3In], [z5C], zdnp, or is selected from Table BA-1.

515. The oligonucleotide of any one of the preceding Embodiments, wherein nucleobase of N_1 is a modified nucleobase.

516. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_1 is a 2'-F modified sugar.

517. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a sugar comprising no substituent at a position corresponding to 2'−OH of a natural RNA sugar.

518. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a sugar comprising no 2'-substituent.

519. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a natural DNA sugar.

520. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a modified sugar.

521. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a 2'-modified sugar.

522. The oligonucleotide of Embodiment 521, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

523. The oligonucleotide of Embodiment 521, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl.

524. The oligonucleotide of Embodiment 521, wherein the modified sugar is a 2'-OMe modified sugar.

525. The oligonucleotide of Embodiment 521, wherein the modified sugar is a 2'-MOE modified sugar.

526. The oligonucleotide of Embodiment 521, wherein the modified sugar is a LNA sugar.

527. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is an acyclic sugar.

528. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a (*R*)-GNA sugar.

529. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a (*S*)-GNA sugar.

530. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a (*S*)-GNA sugar.

531. The oligonucleotide of any one of Embodiments 41-515, wherein the sugar of N_1 is a (*S*)-GNA sugar.

532. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-1} is a UNA sugar.

533. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-1} is m1d.

534. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-1} is a 2'-modified sugar.

535. The oligonucleotide of any one of the preceding Embodiments, wherein the sugar of N_{-1} is a 2'-F modified sugar.

536. The oligonucleotide of any one of Embodiments 46-529, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

537. The oligonucleotide of any one of Embodiments 46-529, wherein the modified sugar is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} alkyl.

538. The oligonucleotide of any one of Embodiments 46-529, wherein the modified sugar is a 2'-OMe

modified sugar.

539. The oligonucleotide of any one of Embodiments 46-529, wherein the modified sugar is a 2'-MOE modified sugar.

540. The oligonucleotide of any one of Embodiments 46-529, wherein the modified sugar is a LNA sugar.

541. The oligonucleotide of any one of Embodiments 46-529, wherein the sugar of N_{-1} is a sugar comprising no substituent at a position corresponding to 2'–OH of a natural RNA sugar.

542. The oligonucleotide of any one of Embodiments 46-529, wherein the sugar of N_{-1} is a sugar comprising no 2'-substituent.

543. The oligonucleotide of any one of Embodiments 46-529, wherein the sugar of N_{-1} is a natural DNA sugar.

544. The oligonucleotide of any one of Embodiments 46-529, wherein the sugar of N_{-1} is a natural RNA sugar.

545. The oligonucleotide of any one of the preceding Embodiments, wherein N_1 and N_{-1} are both complementary to their corresponding nucleosides when the oligonucleotide is aligned with a target nucleic acid.

546. The oligonucleotide of any one of the preceding Embodiments, wherein at least one of N_1 and N_{-1} is independently produces a mismatch or a wobble base pairing when the oligonucleotide is aligned with a target nucleic acid.

547. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of N_{-1} is A, T, C, G, U, hypoxanthine, b001U, b002U, b003U, b004U, b005U, b006U, b007U, b008U, b009U, b011U, b012U, b013U, b014U, b015U, b001A, b002A, b003A, b004A, b005A, b006A, b007A, b001G, b002G, b001C, b002C, b003C, b004C, b005C, b006C, b007C, b008C, b009C, b002I, b003I, b004I, b014I, [3nT], [3ne5U], [3nfl5U], [3npry5U], [3ncn5U], [napth6o8A], [ipr6o8A], [c7ln], [c39z48ln], [z2c3ln], [z5C], or zdnp, or is selected from Table BA-1.

548. The oligonucleotide of any one of the preceding Embodiments, wherein the nucleobase of N_{-1} is a modified nucleobase.

549. The oligonucleotide of any one of Embodiments 1-280, wherein the nucleobase of N_{-1} is hypoxanthine.

550. The oligonucleotide of any one of Embodiments 1-280, wherein the nucleobase of N_{-1} is C.

551. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_0 and N_1 is a phosphorothioate internucleotidic linkage.

552. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_0 and N_1 is a *Sp* phosphorothioate internucleotidic linkage.

553. The oligonucleotide of any one of Embodiments 1-552, wherein the internucleotidic linkage between N_0 and N_1 is a PN internucleotidic linkage.

554. The oligonucleotide of any one of Embodiments 1-552, wherein the internucleotidic linkage between

N_0 and N_1 is a phosphoryl guanidine internucleotidic linkage.

555. The oligonucleotide of any one of Embodiments 1-552, wherein the internucleotidic linkage between N_0 and N_1 is a n001 internucleotidic linkage.

556. The oligonucleotide of any one of Embodiments 1-552, wherein the internucleotidic linkage between N_0 and N_1 is a natural phosphate linkage.

557. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_0 and N_{-1} is a phosphorothioate internucleotidic linkage.

558. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_0 and N_{-1} is a *Sp* phosphorothioate internucleotidic linkage.

559. The oligonucleotide of any one of Embodiments 1-556, wherein the internucleotidic linkage between N_0 and N_{-1} is a PN internucleotidic linkage.

560. The oligonucleotide of any one of Embodiments 1-556, wherein the internucleotidic linkage between N_0 and N_{-1} is a phosphoryl guanidine internucleotidic linkage.

561. The oligonucleotide of any one of Embodiments 1-556, wherein the internucleotidic linkage between N_0 and N_{-1} is a n001 internucleotidic linkage.

562. The oligonucleotide of any one of Embodiments 1-556, wherein the internucleotidic linkage between N_0 and N_{-1} is a n006 internucleotidic linkage.

563. The oligonucleotide of any one of Embodiments 1-556, wherein the internucleotidic linkage between N_0 and N_{-1} is a natural phosphate linkage.

564. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-5'-$N_2N_1N_0N_{-1}$–3', wherein N_2 is a nucleoside linked to N_1 by an internucleotidic linkage.

565. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_2 is a modified sugar.

566. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_2 is a 2'-F modified sugar.

567. The oligonucleotide of any one of Embodiments 1-564, wherein sugar of N_2 is a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

568. The oligonucleotide of any one of Embodiments 1-564, wherein sugar of N_2 is a 2'-OMe modified sugar.

569. The oligonucleotide of any one of Embodiments 1-564, wherein sugar of N_2 is a 2'-MOE modified sugar.

570. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_1 and N_2 is a phosphorothioate internucleotidic linkage.

571. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_1 and N_2 is a *Sp* phosphorothioate internucleotidic linkage.

572. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-$N_1N_0N_{-1}N_{-2}$–3',

wherein N_{-2} is a nucleoside linked to N_{-1} by an internucleotidic linkage.

573. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-2} is a modified sugar.

574. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-2} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

575. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-2} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

576. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-2} is a 2'-OMe modified sugar.

577. The oligonucleotide of Embodiment 574, wherein sugar of N_{-2} is a 2'-MOE modified sugar.

578. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a non-negatively charged internucleotidic linkage.

579. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a phosphoryl guanidine internucleotidic linkage.

580. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is n001.

581. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is *R*p n001.

582. The oligonucleotide of Embodiment 580, wherein the internucleotidic linkage between N_{-1} and N_{-2} is *S*p n001.

583. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is n006.

584. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-1} and N_{-2} is *R*p n006.

585. The oligonucleotide of Embodiment 580, wherein the internucleotidic linkage between N_{-1} and N_{-2} is *S*p n006.

586. The oligonucleotide of any one of Embodiments 1-577, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a MsPA linkage.

587. The oligonucleotide of any one of Embodiments 1-577, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a methylphosphonate linkage.

588. The oligonucleotide of any one of Embodiments 1-577, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a natural phosphate linkage.

589. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-$N_1N_0N_{-1}N_{-2}N_{-3}$-3', wherein N_{-3} is a nucleoside linked to N_{-2} by an internucleotidic linkage.

590. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-3} is a modified sugar.

591. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-3} is a 2'-F modified sugar.

592. The oligonucleotide of any one of Embodiments 1-589, wherein sugar of N_{-3} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

593. The oligonucleotide of any one of Embodiments 1-589, wherein sugar of N_{-3} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

594. The oligonucleotide of any one of Embodiments 1-589, wherein sugar of N_{-3} is a 2'-OMe modified sugar.

595. The oligonucleotide of any one of Embodiments 1-589, wherein sugar of N_{-3} is a 2'-MOE modified sugar.

596. The oligonucleotide of any one of the preceding Embodiments, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage.

597. The oligonucleotide of any one of Embodiments 1-595, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a phosphorothioate internucleotidic linkage.

598. The oligonucleotide of any one of Embodiments 1-595, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a PN internucleotidic linkage.

599. The oligonucleotide of any one of Embodiments 1-595, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a phosphoryl guanidine internucleotidic linkage.

600. The oligonucleotide of any one of Embodiments 1-595, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a n001 internucleotidic linkage.

601. The oligonucleotide of any one of Embodiments 1-595, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a n006 internucleotidic linkage.

602. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}$-3', wherein N_{-4} is a nucleoside linked to N_{-3} by an internucleotidic linkage.

603. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-4} is a modified sugar.

604. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

605. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

606. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a 2'-OMe modified sugar.

607. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a 2'-MOE modified sugar.

608. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a 2'-F modified sugar.

609. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a bicyclic sugar.

610. The oligonucleotide of any one of Embodiments 1-602, wherein sugar of N_{-4} is a LNA sugar.

611. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a phosphorothioate internucleotidic linkage.

612. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a *Sp* phosphorothioate internucleotidic linkage.

613. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a natural phosphate linkage.

614. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a PN internucleotidic linkage.

615. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a phosphoryl guanidine internucleotidic linkage.

616. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a n001 internucleotidic linkage.

617. The oligonucleotide of any one of Embodiments 1-610, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a n006 internucleotidic linkage.

618. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}$–3', wherein N_{-5} is a nucleoside linked to N_{-4} by an internucleotidic linkage.

619. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-5} is a modified sugar.

620. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

621. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

622. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a 2'-OMe modified sugar.

623. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a 2'-MOE modified sugar.

624. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a 2'-F modified sugar.

625. The oligonucleotide of any one of Embodiments 1-618, wherein sugar of N_{-5} is a UNA sugar.

626. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a phosphorothioate internucleotidic linkage.

627. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a *Sp* phosphorothioate internucleotidic linkage.

628. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between

N_{-4} and N_{-5} is a natural phosphate linkage.

629. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a PN internucleotidic linkage.

630. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a phosphoryl guanidine internucleotidic linkage.

631. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a n001 internucleotidic linkage.

632. The oligonucleotide of any one of Embodiments 1-624, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a n006 internucleotidic linkage.

633. The oligonucleotide of any one of the preceding Embodiments, comprising 5'-$N_1N_0N_{-1}N_{-2}N_{-3}N_{-4}N_{-5}N_{-6}$-3', wherein N_{-6} is a nucleoside linked to N_{-5} by an internucleotidic linkage.

634. The oligonucleotide of any one of the preceding Embodiments, wherein sugar of N_{-6} is a modified sugar.

635. The oligonucleotide of any one of Embodiments 1-633, wherein sugar of N_{-6} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

636. The oligonucleotide of any one of Embodiments 1-633, wherein sugar of N_{-6} is a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

637. The oligonucleotide of any one of Embodiments 1-633, wherein sugar of N_{-6} is a 2'-OMe modified sugar.

638. The oligonucleotide of any one of Embodiments 1-633, wherein sugar of N_{-6} is a 2'-MOE modified sugar.

639. The oligonucleotide of any one of Embodiments 1-633, wherein sugar of N_{-6} is a 2'-F modified sugar.

640. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a PN internucleotidic linkage.

641. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a phosphoryl guanidine internucleotidic linkage.

642. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a n001 internucleotidic linkage.

643. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a *R*p n001 internucleotidic linkage.

644. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a n006 internucleotidic linkage.

645. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a *R*p n006 internucleotidic linkage.

646. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between

N_{-5} and N_{-6} is a phosphorothioate internucleotidic linkage.

647. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a *Sp* phosphorothioate internucleotidic linkage.

648. The oligonucleotide of any one of Embodiments 1-639, wherein the internucleotidic linkage between N_{-5} and N_{-6} is a natural phosphate linkage.

649. The oligonucleotide of any one of the preceding Embodiments, wherein N_{-6} is the last nucleoside from the 5'-end.

650. The oligonucleotide of any one of the preceding Embodiments, wherein about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80% of its sugars are each independently a 2'-F modified sugar.

651. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-60% of its sugars are each independently a 2'-F modified sugar.

652. The oligonucleotide of any one of the preceding Embodiments, wherein about 20%-80%, 30-70%, 30%-60%, 30%-50%, 40%-60%, 20%, 30%, 40%, 50%, 60%, 70% or 80% of its sugars are each independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

653. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-60% of its sugars are each independently a 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic.

654. The oligonucleotide of any one of the preceding Embodiments, wherein about 30%-60% of its sugars are each independently a 2'-OMe or 2'-MOE modified sugar.

655. The oligonucleotide of any one of the preceding Embodiments, wherein at least 60%, 70%, 80% or 90% or all natural phosphate linkages each independently bond to at least one modified sugar which is 2'-OR modified sugar wherein R is optionally substituted C_{1-6} aliphatic or a bicyclic sugar.

656. The oligonucleotide of any one of the preceding Embodiments, wherein about 5%-90%, about 10-80%, about 10-75%, about 10-70%, 10%-60%, 10-50%, 10-40%, 10-30%, 15-40%, 20-30%, 25-30%, or about or at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50%, of all internucleotidic linkages in an oligonucleotide are independently a natural phosphate linkage.

657. The oligonucleotide of any one of the preceding Embodiments, wherein there are 5 or more nucleosides at the 3' side of N_0.

658. The oligonucleotide of any one of the preceding Embodiments, wherein there are 5 or more (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 or more) nucleosides at the 5' side of N_0.

659. The oligonucleotide of any one of the preceding Embodiments, wherein there are 20 or more nucleosides at the 5' side of N_0.

660. The oligonucleotide of any one of the preceding Embodiments, wherein there are 21 or more nucleosides at the 5' side of N_0.

661. The oligonucleotide of any one of the preceding Embodiments, wherein there are 22 or more

nucleosides at the 5' side of N_0.

662. The oligonucleotide of any one of the preceding Embodiments, wherein there are 23 or more nucleosides at the 5' side of N_0.

663. The oligonucleotide of any one of the preceding Embodiments, wherein the first 1, 2, 3, 4, 5 or more sugars at the 5'-end of the oligonucleotide are each independently sugars that can increase stability.

664. The oligonucleotide of any one of the preceding Embodiments, wherein the first 1, 2, 3, 4, or 5 sugars at the 5'-end of the oligonucleotide are each independently selected from a bicyclic sugar and a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

665. The oligonucleotide of any one of the preceding Embodiments, wherein the first 1, 2, 3, 4, or 5 sugars at the 5'-end of the oligonucleotide are each independently a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

666. The oligonucleotide of any one of the preceding Embodiments, wherein the first 1, 2, 3, 4, or 5 sugars at the 5'-end of the oligonucleotide are each independently a 2'-OMe or 2'-MOE modified sugar.

667. The oligonucleotide of any one of the preceding Embodiments, wherein the last 1, 2, 3, 4, or 5 sugars at the 3'-end of the oligonucleotide are each independently sugars that can increase stability.

668. The oligonucleotide of any one of the preceding Embodiments, wherein the last 1, 2, 3, 4, or 5 sugars at the 3'-end of the oligonucleotide are each independently selected from a bicyclic sugar and a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

669. The oligonucleotide of any one of the preceding Embodiments, wherein the last 1, 2, 3, 4, or 5 sugars at the 3'-end of the oligonucleotide are each independently a 2'-OR modified sugar, wherein R is optionally substituted C_{1-6} aliphatic.

670. The oligonucleotide of any one of the preceding Embodiments, wherein the last 1, 2, 3, 4, or 5 sugars at the 3'-end of the oligonucleotide are each independently a 2'-OMe or 2'-MOE modified sugar.

671. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is a non-negatively charged internucleotidic linkage.

672. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is a neutral internucleotidic linkage.

673. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is PN internucleotidic linkage.

674. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is phosphoryl guanidine internucleotidic linkage.

675. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is n001 internucleotidic linkage.

676. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is n001.

677. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic

linkage from the 5'-end of an oligonucleotide is n006 internucleotidic linkage.

678. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is n006.

679. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end of an oligonucleotide is a phosphorothioate internucleotidic linkage.

680. The oligonucleotide of any one of the preceding Embodiments, wherein the first internucleotidic linkage from the 5'-end is chirally controlled and is *R*p.

681. The oligonucleotide of any one of Embodiments 1-679, wherein the first internucleotidic linkage from the 5'-end is chirally controlled and is *S*p.

682. The oligonucleotide of any one of the preceding Embodiments, wherein each phosphorothioate internucleotidic linkage is chirally controlled.

683. The oligonucleotide of Embodiment 682, wherein each phosphorothioate internucleotidic linkage is *S*p.

684. An oligonucleotide comprising a duplexing region and a targeting region, wherein a targeting region is or comprises a second region of any one of the preceding Embodiments.

685. An oligonucleotide comprising a duplexing region and a targeting region, wherein a targeting region is or comprises 5'-$N_1N_0N_{-1}$-3' of any one of the preceding Embodiments.

686. The oligonucleotide of any one of Embodiments 684-685, wherein a duplexing region is capable of forming a duplex with a nucleic acid (a duplexing nucleic acid).

687. The oligonucleotide of any one of Embodiments 684-686, wherein a targeting region is capable of forming a duplex with a target nucleic acid comprising a target adenosine.

688. The oligonucleotide of any one of Embodiments 684-687, wherein a duplexing nucleic acid is not a target nucleic acid.

689. The oligonucleotide of any one of Embodiments 684-687, wherein the oligonucleotide is an oligonucleotide of any one of Embodiments 29-683.

690. The oligonucleotide of any one of Embodiments 684-689, wherein the length of a targeting region is about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 nucleosides.

691. The oligonucleotide of any one of Embodiments 684-690, wherein the length of a duplexing region is about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 nucleosides.

692. The oligonucleotide of any one of Embodiments 684-691, wherein the length of a duplexing oligonucleotide is about or at least about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 nucleosides.

693. The oligonucleotide of any one of Embodiments 684-692, wherein a duplexing oligonucleotide comprises a step loop.

694. The oligonucleotide of any one of Embodiments 684-693, wherein the duplexing oligonucleotide comprises one or more modified sugars and one or more modified internucleotidic linkages.

695. The oligonucleotide of any one of Embodiments 684-694, wherein the majority of or all sugars in the duplexing oligonucleotide are modified sugars.

696. The oligonucleotide of any one of Embodiments 684-694, wherein the majority of or all sugars in the duplexing oligonucleotide are 2'-F modified sugars.

697. The oligonucleotide of any one of Embodiments 684-694, wherein the majority of or all sugars in the duplexing oligonucleotide are 2'-OR modified sugars, wherein R is optionally substituted C_{1-6} aliphatic.

698. The oligonucleotide of any one of Embodiments 684-694, wherein the majority of or all sugars in the duplexing oligonucleotide are 2'-OMe modified sugars

699. The oligonucleotide of any one of Embodiments 684-698, wherein the majority of or all internucleotidic linkages in the duplexing oligonucleotide are modified.

700. The oligonucleotide of any one of Embodiments 684-699, wherein the majority of or all internucleotidic linkages in the duplexing oligonucleotide are phosphorothioate internucleotidic linkages.

701. The oligonucleotide of any one of Embodiments 684-700, wherein the duplexing oligonucleotide is chirally controlled.

702. The oligonucleotide of any one of Embodiments 684-701, wherein the majority of or all internucleotidic linkages in the duplexing oligonucleotide are *Sp* phosphorothioate internucleotidic linkages.

703. The oligonucleotide of any one of Embodiments 684-702, wherein the oligonucleotide and its duplexing oligonucleotide are administered as a duplex.

704. The oligonucleotide of any one of Embodiments 684-702, wherein the oligonucleotide and its duplexing oligonucleotide are administered separately.

705. The oligonucleotide of any one of the preceding Embodiments, wherein each PN linkage is independently a phosphoryl guanidine linkage.

706. The oligonucleotide of any one of the preceding Embodiments, wherein each PN linkage is independently n001.

707. The oligonucleotide of any one of the preceding Embodiments, wherein each PN linkage is independently n006.

708. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, a PN internucleotidic linkage, a methylphosphonate internucleotidic linkage and a phosphorothioate internucleotidic linkage.

709. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, a non-negatively charged internucleotidic linkage, and a phosphorothioate internucleotidic linkage.

710. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, a neutral internucleotidic linkage, and a

phosphorothioate internucleotidic linkage.

711. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, a phosphoryl guanidine internucleotidic linkage, a methylphosphonate internucleotidic linkage, and a phosphorothioate internucleotidic linkage.

712. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, n001, n006, a methylphosphonate internucleotidic linkage and a phosphorothioate internucleotidic linkage.

713. The oligonucleotide of any one of the preceding Embodiments, wherein each internucleotidic linkage is independently selected from a natural phosphate linkage, n001, a methylphosphonate internucleotidic linkage and a phosphorothioate internucleotidic linkage.

714. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a salt form.

715. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a pharmaceutically acceptable salt form.

716. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a sodium salt form.

717. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in an ammonium salt form.

718. The oligonucleotide of any one of the preceding Embodiments, wherein the diastereopurity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus.

719. The oligonucleotide of any one of the preceding Embodiments, wherein the diastereopurity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about or at least about 95% and nc is the number of chiral linkage phosphorus.

720. The oligonucleotide of any one of the preceding Embodiments, wherein diastereomeric excess of one or more (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) chiral linkage phosphorus centers is independently about or at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%.

721. The oligonucleotide of any one of the preceding Embodiments, wherein diastereomeric excess of one or more (e.g., 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 or more) chiral linkage phosphorus centers is independently about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%.

722. The oligonucleotide of any one of the preceding Embodiments, wherein diastereomeric excess of each phosphorothioate linkage phosphorus is independently about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%.

723. The oligonucleotide of any one of the preceding Embodiments, wherein diastereomeric excess of

each chiral linkage phosphorus centers is independently about or at least about 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99%.

724. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide has a purity of about 10%-100% (e.g., about 10%-95%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, or about or at least about 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.).

725. The oligonucleotide of any one of Embodiments 29-724, wherein the first domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

726. The oligonucleotide of any one of Embodiments 29-725, wherein the first domain has a length of about 10-25 nucleobases.

727. The oligonucleotide of any one of Embodiments 29-726, wherein the first domain has a length of about 15 nucleobases.

728. The oligonucleotide of any one of Embodiments 29-727, wherein the first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

729. The oligonucleotide of any one of Embodiments 29-728, wherein the first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

730. The oligonucleotide of any one of Embodiments 29-729, wherein the first domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobble pairs when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

731. The oligonucleotide of any one of Embodiments 29-730, wherein the first domain is fully complementary to a target PNPLA3 transcript.

732. The oligonucleotide of any one of Embodiments 29-731, wherein the first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) sugars with 2'-F modification.

733. The oligonucleotide of any one of Embodiments 29-732, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%,

80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in the first domain independently comprise a 2'-F modification.

734. The oligonucleotide of any one of Embodiments 29-733, wherein about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of sugars in the first domain independently comprise a 2'-F modification.

735. The oligonucleotide of any one of Embodiments 29-734, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain independently comprise a 2'-F modification.

736. The oligonucleotide of any one of Embodiments 29-735, wherein no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain comprises 2'-OMe.

737. The oligonucleotide of any one of Embodiments 29-736, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain comprises 2'-OMe.

738. The oligonucleotide of any one of Embodiments 29-737, wherein no more than about 50% of sugars in the first domain comprises 2'-OMe.

739. The oligonucleotide of any one of Embodiments 29-738, wherein no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic.

740. The oligonucleotide of any one of Embodiments 29-739, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic.

741. The oligonucleotide of any one of Embodiments 29-740, wherein no more than about 50% of sugars in the first domain comprises 2'-OR, wherein R is optionally substituted C_{1-6} aliphatic.

742. The oligonucleotide of any one of Embodiments 29-741, wherein no more than about 1%-95% (e.g., no more than about 1%, 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, etc.) of sugars in the first domain comprises 2'-OR.

743. The oligonucleotide of any one of Embodiments 29-742, wherein about 30%-70% (e.g., about 30%-60%, 30%-50%, or about 30%, 40%, 50%, 60% or 70%) of sugars in the first domain comprises 2'-OR, wherein R is not –H.

744. The oligonucleotide of any one of Embodiments 29-743, wherein no more than about 50% of sugars in the first domain comprises 2'-OR.

745. The oligonucleotide of any one of Embodiments 29-744, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OR modification, wherein R is optionally substituted C_{1-6} aliphatic.

746. The oligonucleotide of any one of Embodiments 29-745, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-MOE modification.

747. The oligonucleotide of any one of Embodiments 29-746, wherein the first domain comprises one or more (e.g., about 1-20, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, etc.) modified sugars comprising a 2'-OMe modification.

748. The oligonucleotide of any one of Embodiments 29-747, wherein the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-OR modified sugar, wherein R is independently optionally substituted C_{1-6} aliphatic.

749. The oligonucleotide of any one of Embodiments 29-748, wherein the first about 1-5, e.g., 1, 2, 3, 4, or 5 sugars from the 5'-end of a first domain is independently a 2'-MOE modified sugar.

750. The oligonucleotide of any one of Embodiments 29-749, wherein the first domain comprises a PS internucleotidic linkage and a PN internucleotidic linkage.

751. The oligonucleotide of any one of Embodiments 29-750, wherein each internucleotidic linkage in the first domain is independently a PO internucleotidic linkage, a PS internucleotidic linkage or a PN internucleotidic linkage.

752. The oligonucleotide of any one of Embodiments 29-751, wherein the first domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified internucleotidic linkages.

753. The oligonucleotide of any one of Embodiments 29-752, wherein about 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of internucleotidic linkages in the first domain are modified internucleotidic linkages.

754. The oligonucleotide of any one of Embodiments 29-753, wherein about 50%-100% (e.g., about 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%,

etc.) of internucleotidic linkages in the first domain are modified internucleotidic linkages.

755. The oligonucleotide of any one of Embodiments 29-754, wherein each modified internucleotidic linkages is independently a chiral internucleotidic linkage.

756. The oligonucleotide of any one of Embodiments 29-755, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a non-negatively charged internucleotidic linkage.

757. The oligonucleotide of any one of Embodiments 29-756, wherein each modified internucleotidic linkages is independently a phosphorothioate internucleotidic linkage or a neutral internucleotidic linkage.

758. The oligonucleotide of any one of Embodiments 29-757, wherein the first domain comprises one or more phosphorothioate internucleotidic linkages.

759. The oligonucleotide of any one of Embodiments 29-758, wherein the first domain comprises 1, 2, 3, 4, or 5 non-negatively charged internucleotidic linkages.

760. The oligonucleotide of any one of Embodiments 29-759, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is a non-negatively charged internucleotidic linkage.

761. The oligonucleotide of any one of Embodiments 29-760, wherein at least 5%-100% (e.g., about 10%-100%, 20-100%, 30%-100%, 40%-100%, 50%-80%, 50%-85%, 50%-90%, 50%-95%, 60%-80%, 60%-85%, 60%-90%, 60%-95%, 60%-100%, 65%-80%, 65%-85%, 65%-90%, 65%-95%, 65%-100%, 70%-80%, 70%-85%, 70%-90%, 70%-95%, 70%-100%, 75%-80%, 75%-85%, 75%-90%, 75%-95%, 75%-100%, 80%-85%, 80%-90%, 80%-95%, 80%-100%, 85%-90%, 85%-95%, 85%-100%, 90%-95%, 90%-100%, 10%, 20%, 30%, 40%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100%, etc.) of chiral internucleotidic linkages in the first domain is *S*p.

762. The oligonucleotide of any one of Embodiments 34-761, wherein the internucleotidic linkage between the first and the second nucleosides of the first domain is *R*p.

763. The oligonucleotide of any one of Embodiments 34-762, wherein the internucleotidic linkage between the last and the second last nucleosides of the first domain is *R*p.

764. The oligonucleotide of any one of Embodiments 29-763, wherein each internucleotidic linkage in the first domain is independently a modified internucleotidic linkage.

765. The oligonucleotide of any one of Embodiments 29-764, wherein the first domain can recruit, or promotes or contributes to recruitment of, an ADAR protein to a target PNPLA3 transcript.

766. The oligonucleotide of any one of Embodiments 29-765, wherein the second domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

767. The oligonucleotide of any one of Embodiments 29-766, wherein the second domain has a length of about 5-15 nucleobases.

768. The oligonucleotide of any one of Embodiments 29-767, wherein the second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

769. The oligonucleotide of any one of Embodiments 29-768, wherein the second domain comprises two or more mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

770. The oligonucleotide of any one of Embodiments 1-116, wherein the second domain comprises one and no more than one mismatch when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

771. The oligonucleotide of any one of Embodiments 1-116, wherein the second domain comprises two and no more than two mismatches when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

772. The oligonucleotide of any one of Embodiments 29-771, wherein the second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) bulges when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

773. The oligonucleotide of Embodiment 125, wherein each bulge independently comprises one or more base pairs that are not Watson-Crick or wobble pairs.

774. The oligonucleotide of any one of Embodiments 29-773, wherein the second domain comprises one or more (e.g., 1-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) wobble pairs when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

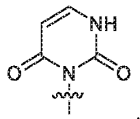
775. The oligonucleotide of any one of Embodiments 29-774, wherein the second domain comprise a nucleoside opposite to a target adenosine when the oligonucleotide is aligned with a target PNPLA3 transcript for complementarity.

776. The oligonucleotide of Embodiment 131, wherein the opposite nucleobase is optionally substituted or protected U, or is an optionally substituted or protected tautomer of U.

777. The oligonucleotide of Embodiment 131, wherein the opposite nucleobase is U.

778. The oligonucleotide of any one of Embodiments 29-777, wherein the oligonucleotide comprises a nucleobase BA, wherein BA is or comprises Ring BA or a tautomer thereof, wherein Ring BA is an optionally substituted, 5-20 membered, monocyclic, bicyclic or polycyclic ring having 0-10 heteroatoms.

779. The oligonucleotide of any one of Embodiments 140-150, wherein Ring BA has the structure of



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780. The oligonucleotide of any one of Embodiments 29-779, wherein the second domain comprises about 1-50 (e.g., about 5, 6, 7, 8, 9, or 10 – about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25,

30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc., about 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20, etc.) modified sugars independently with a modification that is not 2'-F.

781. The oligonucleotide of any one of the preceding Embodiments, wherein the target adenosine is at a position within the PNPLA3 transcript encoding for an amino acid at position 148 of a PNPLA3 polypeptide.

782. The oligonucleotide of any one of the preceding Embodiments, wherein the target adenosine is at a position within the PNPLA3 transcript encoding for an amino acid at position 148 of SEQ ID NO: 2.

783. The oligonucleotide of Embodiment 781, wherein the amino acid is methionine.

784. The oligonucleotide of any one of Embodiments 29-783, wherein second domain comprises a PS internucleotidic linkage and a PN internucleotidic linkage.

785. The oligonucleotide of any one of Embodiments 29-784, wherein each internucleotidic linkage in the second domain is independently a PO internucleotidic linkage, a PS internucleotidic linkage or a PN internucleotidic linkage.

786. The oligonucleotide of any one of the preceding Embodiments, wherein each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage.

787. The oligonucleotide of any one of the preceding Embodiments, wherein each PS internucleotidic linkage is independently a *Sp* phosphorothioate internucleotidic linkage.

788. The oligonucleotide of any one of the preceding Embodiments, wherein each PN internucleotidic linkage is independently a phosphoryl guanidine internucleotidic linkage.

789. The oligonucleotide of any one of the preceding Embodiments, wherein each PN internucleotidic linkage is independently a n001 internucleotidic linkage.

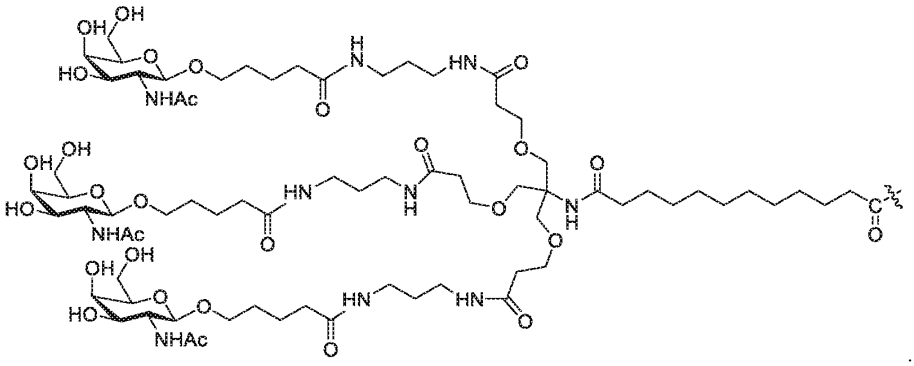
790. The oligonucleotide of any one of the preceding Embodiments, wherein each PN internucleotidic linkage is independently a n006 internucleotidic linkage.

791. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide comprises an additional chemical moiety.

792. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide comprises an asialoglycoprotein receptor ligand.

793. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide comprises GalNAc.

794. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide



comprises .

795. The oligonucleotide of Embodiment 794, wherein the –C(O)– is bonded to the oligonucleotide chain through a linker.

796. The oligonucleotide of Embodiment 794, wherein the linker is or comprises L001

797. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a pharmaceutically acceptable salt form.

798. The oligonucleotide of any one of the preceding Embodiments, wherein the number of chiral linkage phosphorus in the oligonucleotide is about or at least about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30.

799. An oligonucleotide of Table 1.

800. An oligonucleotide, wherein the oligonucleotide is ADR-0110420.

801. An oligonucleotide, wherein the oligonucleotide is ADR-0110652.

802. An oligonucleotide, wherein the oligonucleotide is ADR-0110667.

803. An oligonucleotide, wherein the oligonucleotide is ADR-0110481.

804. An oligonucleotide, wherein the oligonucleotide is ADR-0111148.

805. An oligonucleotide, wherein the oligonucleotide is ADR-0111146.

806. An oligonucleotide, wherein the oligonucleotide is ADR-0111820.

807. An oligonucleotide, wherein the oligonucleotide is ADR-0111776.

808. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a pharmaceutically acceptable salt form.

809. The oligonucleotide of any one of the preceding Embodiments, wherein the oligonucleotide is in a sodium salt form.

810. An oligonucleotide, wherein the oligonucleotide is an oligonucleotide selected from:

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0; and

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0,

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ss

p].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

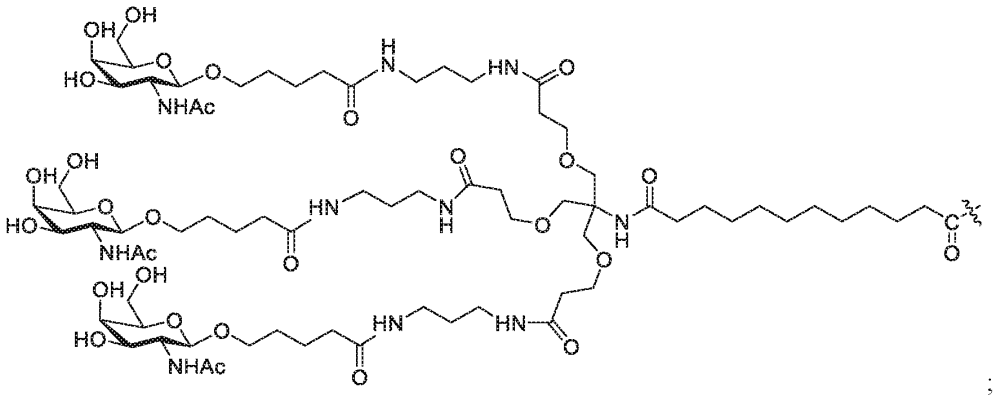
RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

or a salt thereof, wherein:

[GalNAc3C12oyl] represents



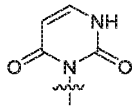
;

[nC6o] represents $-NH(CH_2)_6-$, wherein –NH– is bonded to [GalNAc3C12oyl], and the end $-CH_2-$ is bonded to an oxygen atom that is bonded to the linkage phosphorus of a phosphate linkage;

d represents a natural DNA sugar in a nucleoside;

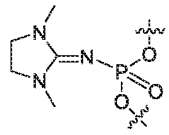
m represents a 2'-OMe modified sugar in a nucleoside;

[fl2r] represents a 2'-F modified sugar in a nucleoside;

[3nU] represents a nucleoside whose base is ;

p represents a phosphate linkage;

[Ssp] represents a phosphorothioate linkage in the *S*p configuration; and

[n001R] represents  wherein the phosphorus is of the *R*p configuration.

811. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

812. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

813. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

814. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

815. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

816. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

817. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

818. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

819. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

820. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

821. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

822. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

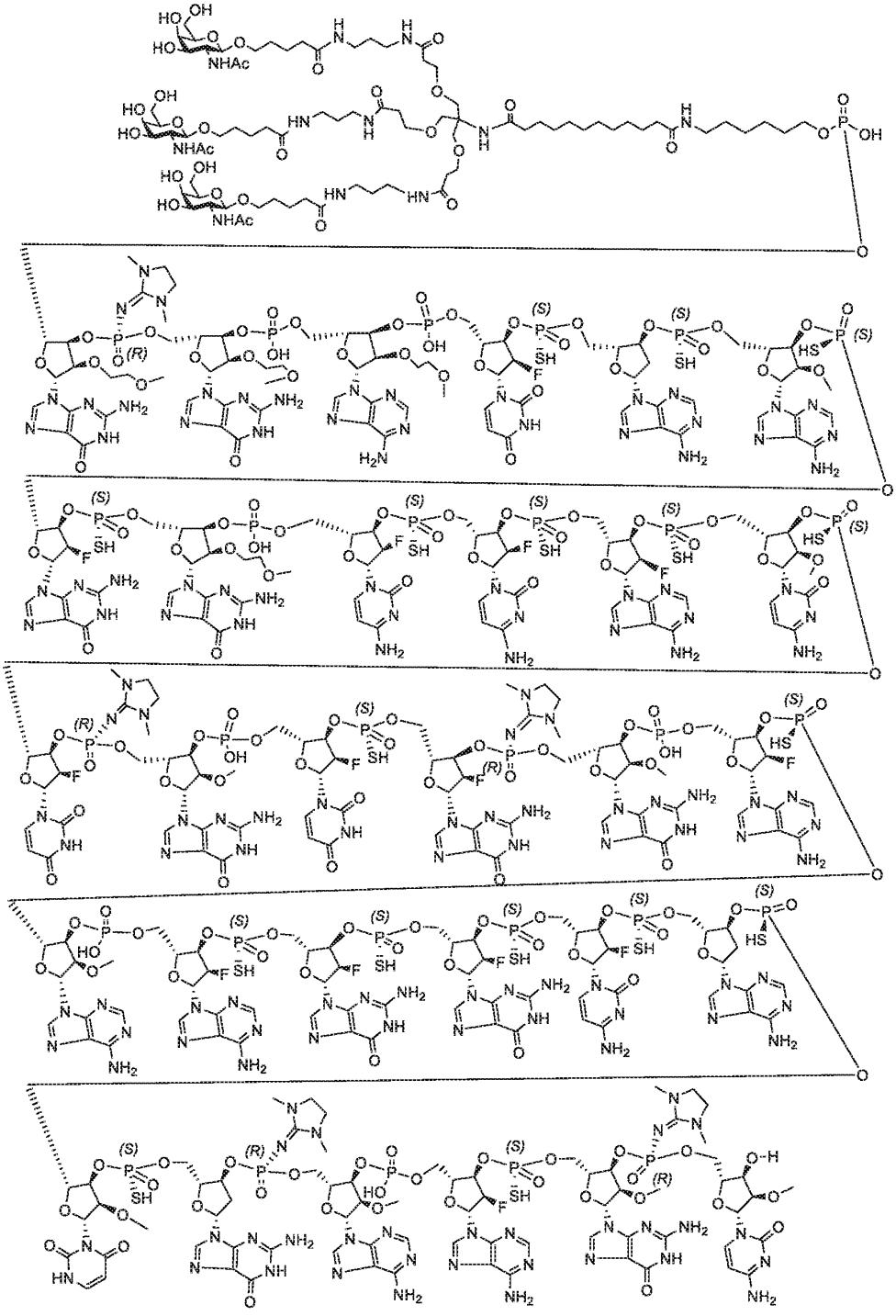
823. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

824. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

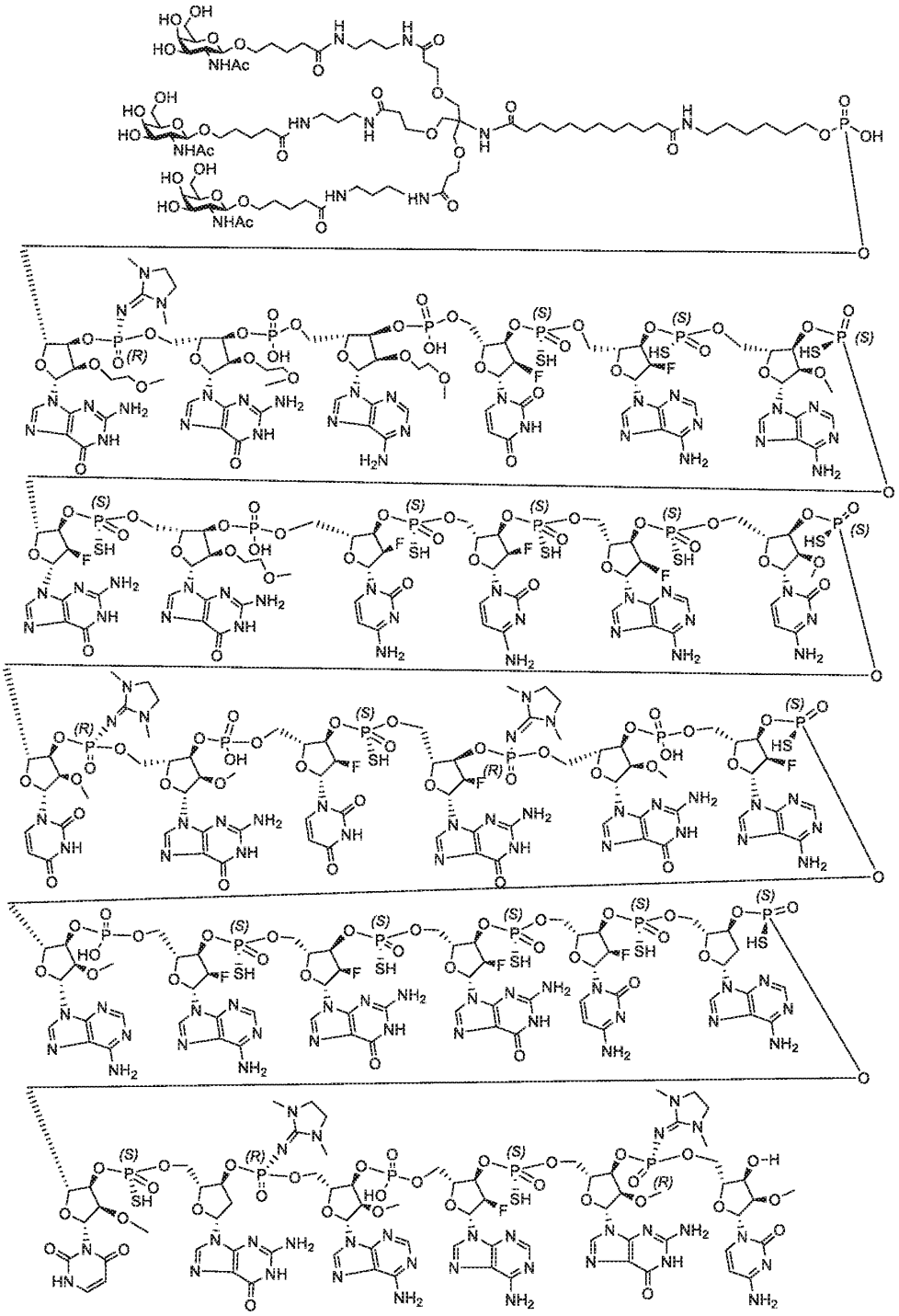
825. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

826. The oligonucleotide of Embodiment 810, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

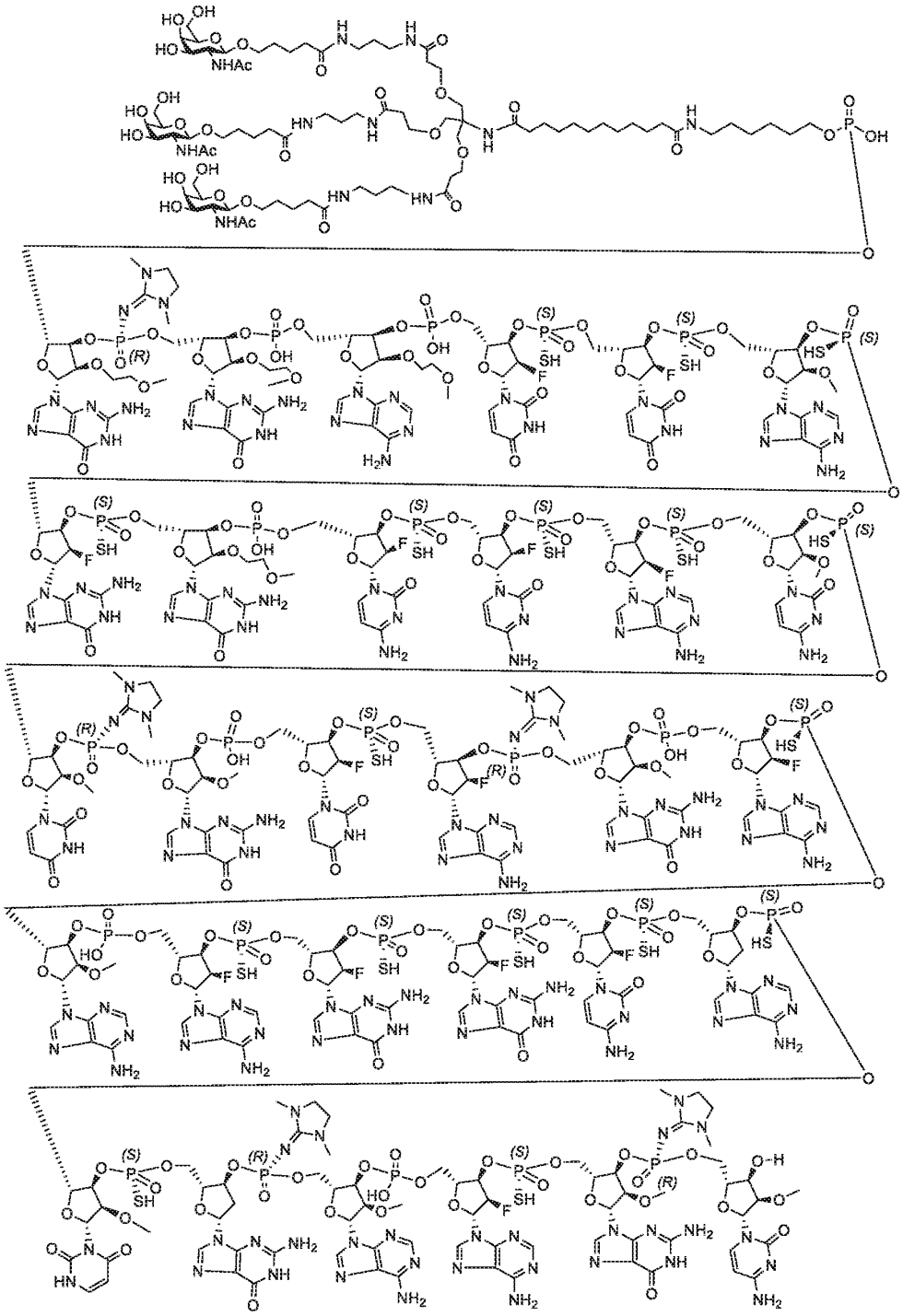
827. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



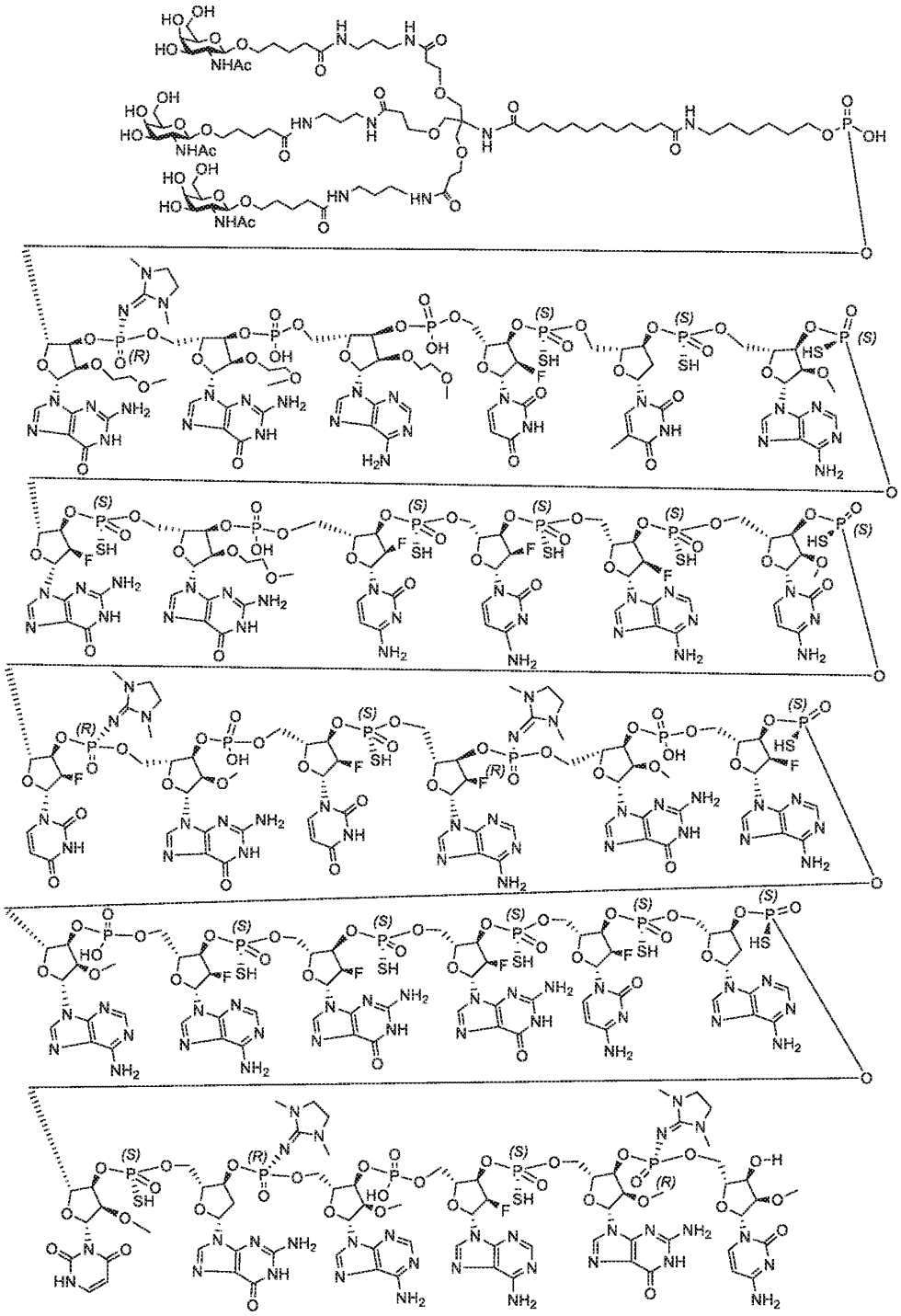
828. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



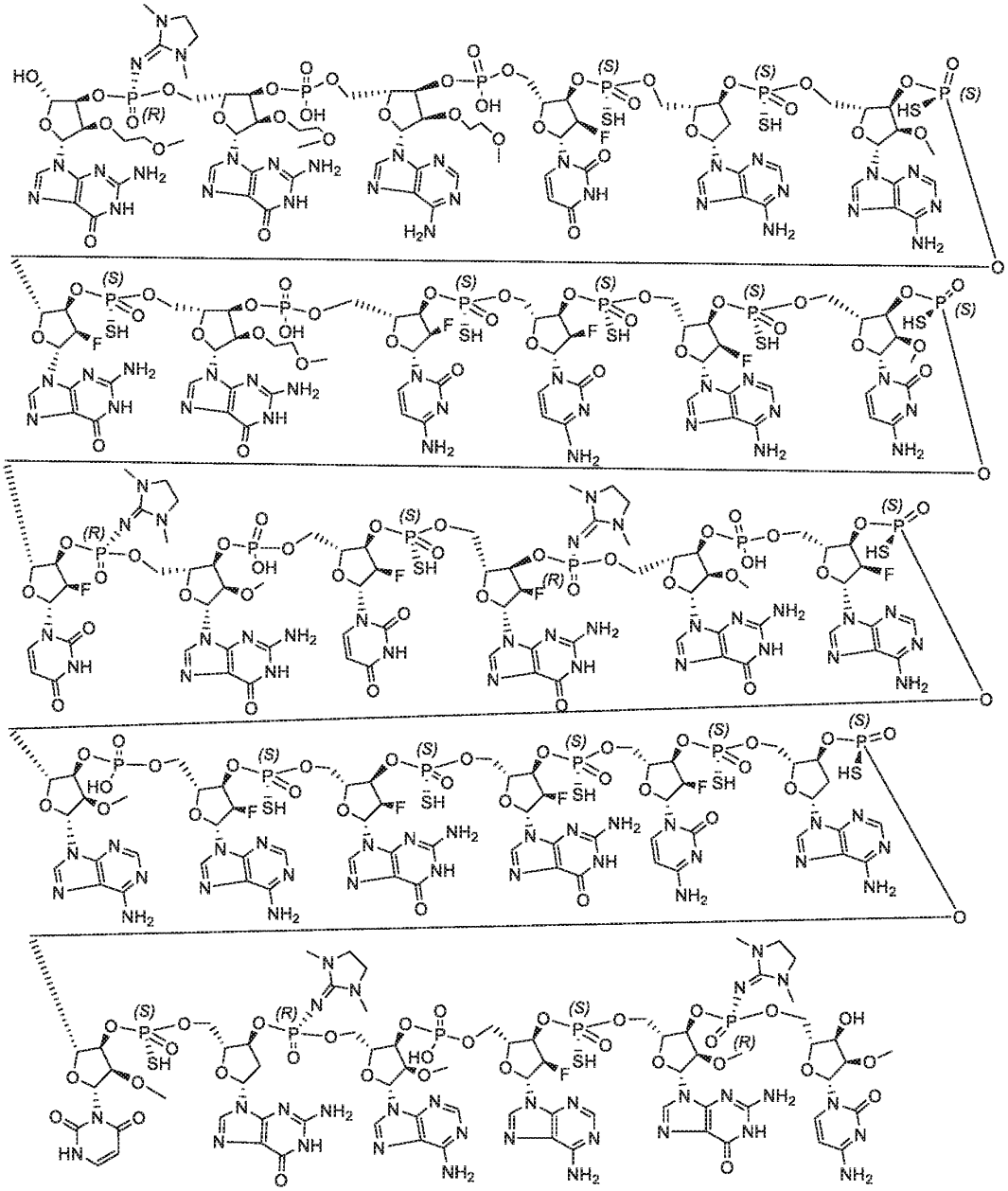
829. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



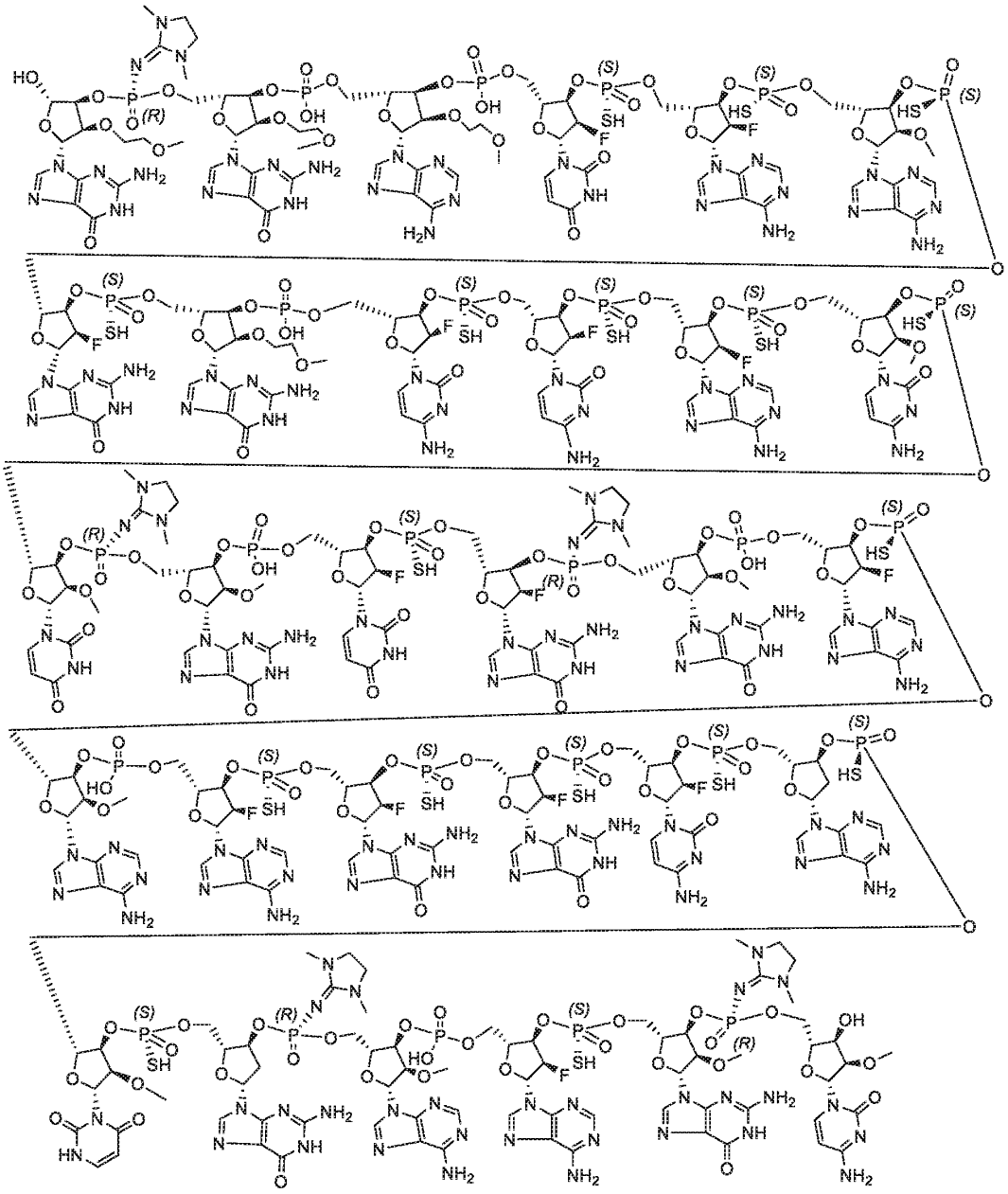
830. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



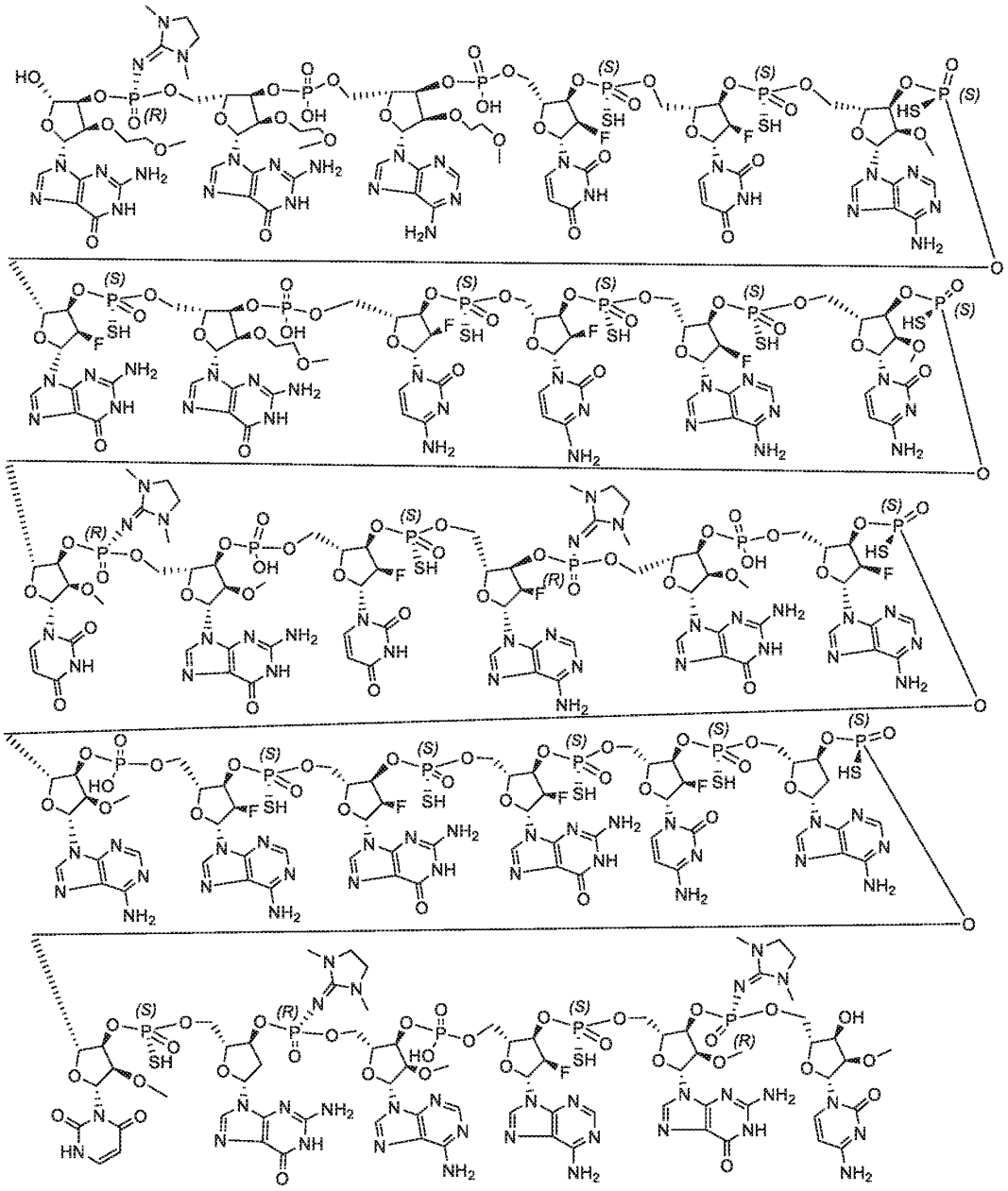
831. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



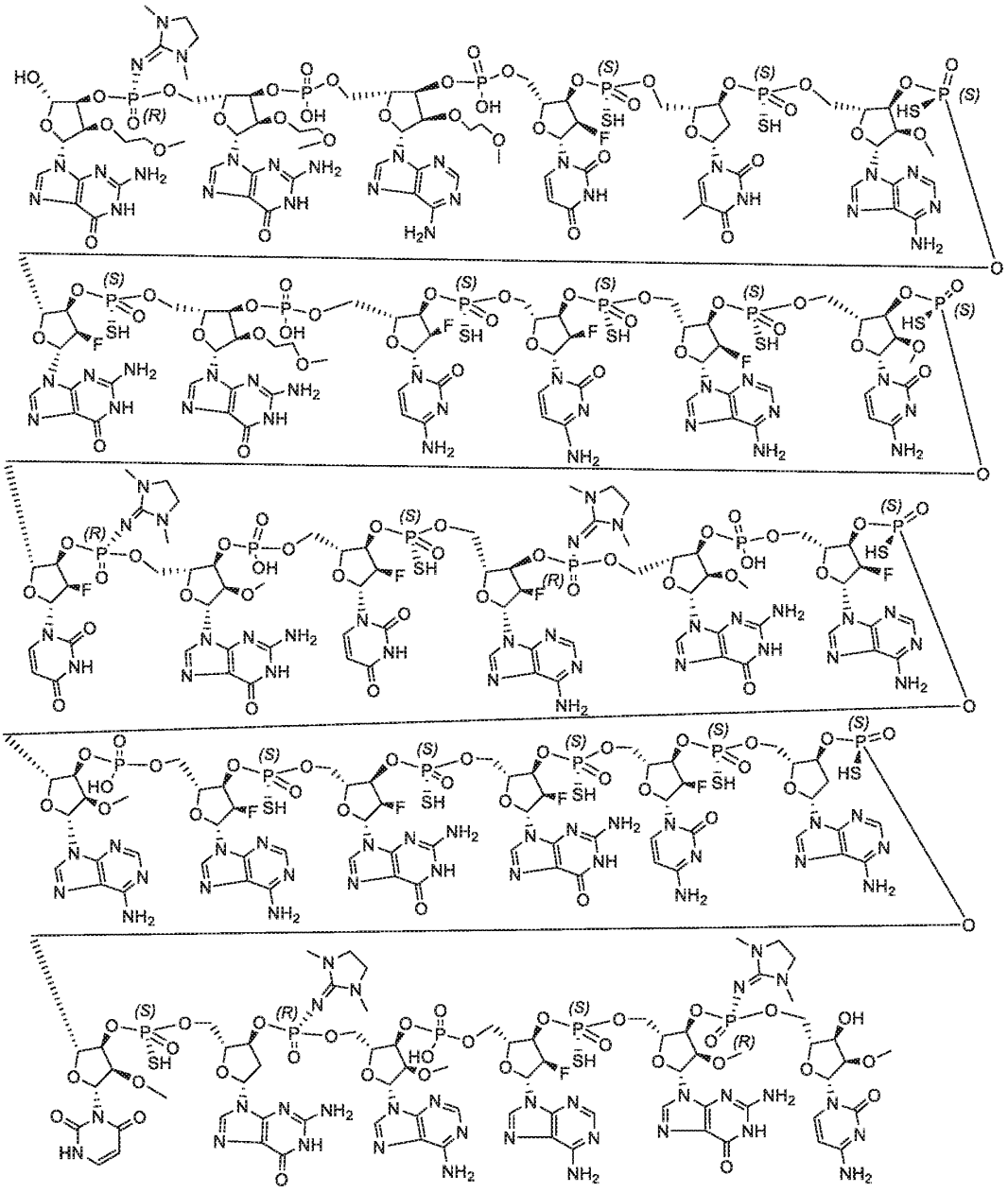
832. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



833. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



834. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



835. An oligonucleotide, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one of the preceding Embodiments.

836. An oligonucleotide, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one of Embodiments 810-834.

837. An oligonucleotide, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one

of the preceding Embodiments with respect to a chiral linkage phosphorus.

838. An oligonucleotide, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one of Embodiments 810-834 with respect to a chiral linkage phosphorus.

839. The oligonucleotide of any one of Embodiments 835-838, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one of Embodiments 810-834 with respect to a PN chiral linkage phosphorus.

840. The oligonucleotide of any one of Embodiments 835-839, wherein the oligonucleotide is a diastereomer of an oligonucleotide of any one of Embodiments 810-834 with respect to a PS chiral linkage phosphorus.

841. The oligonucleotide of any one of Embodiments 835-840, wherein the diastereomer differs from an oligonucleotide of any one of Embodiments 810-834 only at chiral linkage phosphorus.

842. The oligonucleotide of any one of Embodiments 835-840, wherein the diastereomer differs from an oligonucleotide of any one of Embodiments 810-834 only at a single chiral linkage phosphorus.

843. The oligonucleotide of any one of Embodiments 810-842, wherein the oligonucleotide is a salt of the compound.

844. The oligonucleotide of any one of Embodiments 810-842, wherein the oligonucleotide is a pharmaceutically acceptable salt of the compound.

845. The oligonucleotide of any one of Embodiments 810-842, wherein the oligonucleotide is a sodium salt of the compound.

846. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral linkage phosphorus independently has a diastereomeric purity of about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%.

847. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral linkage phosphorus independently has a diastereomeric purity of about or at least about 90%.

848. The oligonucleotide of any one of the preceding Embodiments, wherein each chiral linkage phosphorus independently has a diastereomeric purity of about or at least about 95%.

849. The oligonucleotide of any one of the preceding Embodiments, wherein the diastereomeric purity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%), and nc is the number of chiral linkage phosphorus in the oligonucleotide.

850. The oligonucleotide of any one of the preceding Embodiments, wherein the diastereomeric purity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about 95%-100% and nc is the number of chiral linkage phosphorus in the oligonucleotide.

851. The oligonucleotide of any one of the preceding Embodiments, wherein the purity of the oligonucleotide is about 20%-100%, or is about or at least about 20%-95%, 30%-90%, 40%-85%, 40%-80%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, or 90% (e.g., peak area% at 260 nm).

852. A pharmaceutical composition which comprises or delivers an effective amount of an oligonucleotide of any one of the preceding Embodiments or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

853. A pharmaceutical composition comprising an oligonucleotide of any one of the preceding Embodiments and a pharmaceutically acceptable carrier.

854. A pharmaceutical composition that delivers an oligonucleotide of any one of the preceding Embodiments and optionally a pharmaceutically acceptable carrier.

855. The composition of Embodiment 854, wherein the oligonucleotide in the composition comprises a pharmaceutically acceptable salt form.

856. The composition of any one of Embodiments 852-855, wherein each chiral linkage phosphorus of the oligonucleotide independently has a diastereomeric purity of about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%.

857. The composition of any one of Embodiments 852-855, wherein each chiral linkage phosphorus of the oligonucleotide independently has a diastereomeric purity of about or at least about 90%.

858. The composition of any one of Embodiments 852-855, wherein each chiral linkage phosphorus of the oligonucleotide independently has a diastereomeric purity of about or at least about 95%.

859. The composition of any one of the preceding Embodiments, wherein the diastereomeric purity of the oligonucleotide in the composition is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%), and nc is the number of chiral linkage phosphorus in the oligonucleotide.

860. The composition of any one of the preceding Embodiments, wherein the diastereomeric purity of the oligonucleotide in the composition is about or at least about $(DS)^{nc}$, wherein DS is about 95%-100%, and nc is the number of chiral linkage phosphorus in the oligonucleotide.

861. The composition of any one of the preceding Embodiments, wherein the comprises an oligonucleotide of any one of Embodiments oligonucleotide is an oligonucleotide of any one of Embodiments 810-834.

862. The composition of any one of the preceding Embodiments, wherein the comprises an oligonucleotide of any one of Embodiments oligonucleotide is an oligonucleotide of any one of Embodiments 835-842.

863. A composition comprising a plurality of oligonucleotides, wherein each oligonucleotides of the plurality is independently a particular oligonucleotide or a salt thereof, wherein the particular oligonucleotide is an oligonucleotide of any one of the preceding Embodiments.

864. An oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-

40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein each oligonucleotide of the plurality is independently an oligonucleotide of any one of the preceding Embodiments (e.g., in an acid, base, or salt form).

865. An oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein the common base sequence is complementary to a base sequence of a portion of PNPLA3 transcript which portion comprises a target adenosine.

866. The composition of Embodiment 865, wherein the common base sequence is complementary to a base sequence of a portion of a PNPLA3 transcript with 0-10 (e.g., 0-1, 0-2, 0-3, 0-4, 0-5, 0-6, 0-7, 0-8, 0-9, 0-10, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, 2-5, 2-6, 2-7, 2-8, 2-9, 2-10, 3-4, 3-5, 3-6, 3-7, 3-8, 3-9, 3-10, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, etc.) mismatches which are not Watson-Crick base pairs.

867. The composition of Embodiment 866, wherein the common base sequence is complementary to a base sequence of a portion of a PNPLA3 transcript with 0-5 mismatches which are not Watson-Crick base pairs.

868. The composition of Embodiment 865, wherein the common base sequence is 100% complementary to a base sequence of a portion of a PNPLA3 transcript across the length of the common base sequence except the nucleoside opposite to a target adenosine.

869. The composition of Embodiment 865, wherein the common base sequence is 100% complementary to a base sequence of a portion of a PNPLA3 transcript across the length of the common base sequence.

870. The composition of any one of the preceding Embodiments, wherein the portion of a PNPLA3 transcript comprises a target adenosine in a codon encoding an amino acid at position 148 of SEQ ID NO: 1 or 2.

871. The composition of any one of the preceding Embodiments, wherein the portion of a PNPLA3 transcript comprises a target adenosine in a codon encoding an amino acid at position 148 of SEQ ID NO: 2.

872. The composition of any one of Embodiments 864-869, wherein the composition can edit a target A to I when contacted with a PNPLA3 transcript in a system expressing ADAR.

873. The composition of any one of Embodiments 864-872, wherein oligonucleotides of the plurality share the same base and sugar modifications.

874. The composition of any one of Embodiments 864-873, wherein oligonucleotides of the plurality

share the same pattern of backbone chiral centers.

875. The composition of any one of Embodiments 864-874, wherein the composition is enriched for oligonucleotides of the plurality compared to a stereorandom preparation of the oligonucleotides wherein no internucleotidic linkages are chirally controlled.

876. The composition of any one of Embodiments 864-874, wherein a non-random level of all oligonucleotides in the composition that share the common base sequence and the same base and sugar modifications are oligonucleotides of the plurality.

877. The composition of any one of Embodiments 864-874, wherein a non-random level of all oligonucleotides in the composition that share the common base sequence are oligonucleotides of the plurality.

878. The composition of any one of Embodiments 864-877, wherein oligonucleotides of the plurality are of the same oligonucleotide or one or more pharmaceutically acceptable salts thereof.

879. The composition of any one of Embodiments 864-877, wherein oligonucleotides of the plurality are one or more pharmaceutically acceptable salts of the same acid-form oligonucleotide.

880. The composition of any one of Embodiments 864-877, wherein oligonucleotides of the plurality are of the same constitution.

881. The composition of Embodiment 880, wherein a non-random level of all oligonucleotides in the composition that share the same base sequence as oligonucleotides of the plurality are oligonucleotides of the plurality.

882. The composition of Embodiment 880, wherein a non-random level of all oligonucleotides in the composition that share the same constitution are oligonucleotides of the plurality.

883. The composition of any one of Embodiments 864-882, wherein the level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus.

884. The composition of any one of Embodiments 864-882, wherein the level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about 20%-100%, or is about or at least about 20%-95%, 30%-90%, 40%-85%, 40%-80%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, or 90%.

885. The composition of any one of Embodiments 864-877, wherein oligonucleotides of the plurality are of the same structure.

886. The composition of any one of Embodiments 864-885, wherein oligonucleotides of the plurality are sodium salts.

887. The composition of any one of Embodiments 864-886, wherein oligonucleotides of the plurality share the same linkage phosphorus stereochemistry at 10 or more chiral internucleotidic linkages.

888. The composition of any one of Embodiments 864-887, wherein oligonucleotides of the plurality share the same linkage phosphorus stereochemistry at each phosphorothioate internucleotidic linkages.

889. The composition of any one of Embodiments 864-888, wherein oligonucleotides of the plurality do not share the same linkage phosphorus stereochemistry at one or more or any non-negatively charged internucleotidic linkages.

890. The composition of any one of Embodiments 864-888, wherein oligonucleotides of the plurality are each independently an oligonucleotide of any one of Embodiments 810-834.

891. The composition of any one of Embodiments 864-888, wherein the composition comprises an oligonucleotide of any one of Embodiments 835-842.

892. A method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding Embodiments.

893. A method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising converting the amino acid at position 148 of the PNPLA3 polypeptide into a valine.

894. A method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide.

895. A method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide.

896. A method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding Embodiments.

897. A method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide.

898. A method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide.

899. A method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding Embodiments.

900. A method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in PNPLA3 in the genome of a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide.

901. A method for preventing or treating a condition, disorder or disease, comprising editing a target

adenosine in a PNPLA3 transcript in a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide.

902. A method for preventing or treating a condition, disorder or disease, comprising administering or delivering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or composition of any one of the preceding Embodiments.

903. The method of any one of Embodiments 900-902, wherein the condition, disorder or disease is amenable to an A to G or A to I modification.

904. The method of any one of Embodiments 900-903, wherein the condition, disease or disorder is associated with a PNPLA3 I148M mutation.

905. The method of any one of Embodiments 900-903, wherein the condition, disease or disorder is amenable to or can benefit from changing I148M to I148V in PNPLA3.

906. The method of any one of Embodiments 892-903, wherein the subject comprises an I148M mutation in PNPLA3.

907. The method of Embodiment 906, wherein the subject is homozygous for the mutation.

908. The method of Embodiment 906, wherein the subject is heterozygous for the mutation.

909. The method of any one of Embodiments 900-907, wherein the condition, disorder or disease is a liver condition, disorder or disease.

910. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is a metabolic liver condition, disorder or disease.

911. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is hepatitis.

912. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is fibrosis.

913. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is cirrhosis.

914. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is hepatocellular carcinoma (HCC).

915. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is steatosis.

916. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is liver failure.

917. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is metabolic dysfunction-associated steatohepatitis (MASH).

918. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is nonalcoholic steatohepatitis (NASH).

919. The method of any one of Embodiments 900-909, wherein the condition, disorder or disease is non-

alcoholic fatty liver disease (NAFLD).

920. The method of any one of the preceding Embodiments, comprising assessment of liver fat.

921. The method of any one of the preceding Embodiments, comprising assessment of liver fat by MRI-PDFF.

922. The method of any one of the preceding Embodiments, comprising assessment of liver stiffness.

923. The method of any one of the preceding Embodiments, comprising liver biopsy.

924. The method of any one of the preceding Embodiments, comprising liver biopsy histology.

925. The method of any one of Embodiments 900-924, wherein oligonucleotides administered to the subject are GalNAc-conjugated oligonucleotides.

926. A method for modulating a protein interaction with an agent in a system wherein a protein is translated from its encoding RNA, comprising administering to the system an oligonucleotide or composition of any one of the preceding Embodiments, wherein an adenosine in the encoding RNA is edited, wherein a protein is translated from the edited mRNA ("the edited protein"), wherein the edited protein differs from the unedited protein at an amino acid residue involving in the protein-agent interaction.

927. The method of Embodiment 926, wherein an agent is or comprises a small molecule.

928. The method of Embodiment 926, wherein an agent is or comprises a lipid.

929. The method of Embodiment 928, wherein an agent is or comprises a triglyceride.

930. The method of any one of Embodiments 926-929, wherein the protein is PNPLA3 or a variant thereof.

931. The method of any one of the preceding Embodiments, comprising administering or delivering an oligonucleotide of any one of Embodiments 810-834.

932. The method of any one of the preceding Embodiments, comprising administering or delivering an oligonucleotide of any one of Embodiments 835-842.

933. The method of any one of the preceding Embodiments, wherein the oligonucleotide is delivered by administering to the subject an effective amount of a conjugate of the oligonucleotide with an additional chemical moiety or a salt thereof.

934. A method for delivering to a system an oligonucleotide, comprising administering to the system a conjugate of the oligonucleotide with an additional chemical moiety or a salt thereof.

935. The method of Embodiment 934, wherein the system is or comprises a cell.

936. The method of Embodiment 934, wherein the system is or comprises a tissue.

937. The method of Embodiment 934, wherein the system is or comprises an organ.

938. The method of Embodiment 934, wherein the system is a subject.

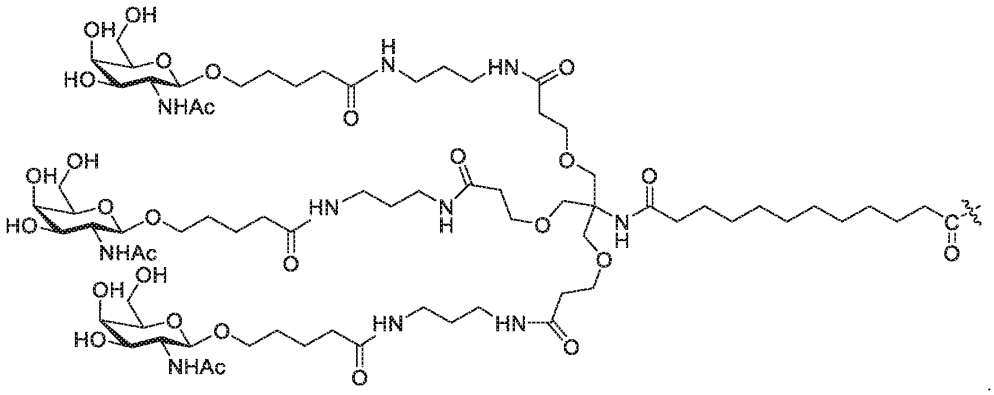
939. The method of Embodiment 934, wherein the system is a human.

940. The method of any one of Embodiments 933-939, wherein the additional chemical moiety is or comprises a targeting moiety.

941. The method of any one of Embodiments 933-940, wherein the additional chemical moiety is or

comprises GalNAc.

942. The method of any one of Embodiments 933-940, wherein the additional chemical moiety is or comprises optionally substituted



943. The method of any one of Embodiments 933-942, wherein the additional chemical moiety is directly conjugated to the oligonucleotide.

944. The method of any one of Embodiments 933-942, wherein the additional chemical moiety is conjugated via a linker to oligonucleotide.

945. The method of Embodiment 944, wherein a linker is or comprises L001.

946. The method of Embodiment 934, comprising delivering an oligonucleotide of any one of Embodiments 811-818 and administering a corresponding oligonucleotide without GalNAc of any one of Embodiments 819-826.

947. The method of Embodiment 934, comprising delivering an oligonucleotide of any one of Embodiments 827-830 and administering a corresponding oligonucleotide without GalNAc of any one of Embodiments 831-834.

948. A method for preparing an oligonucleotide or composition of any one of the preceding Embodiments, comprising utilizing a phosphoramidite (e.g., a phosphoramidite comprising a chiral auxiliary).

949. Use of an oligonucleotide or composition of any one of the preceding Embodiments for editing a target adenosine in a codon.

950. The use of Embodiment 949, wherein sequence, expression, level and/or activity of a protein is altered.

951. Use of an oligonucleotide or composition of any one of Embodiments 29-891, for preventing or treating a condition, disease or disorder.

952. Use of an oligonucleotide or composition of any one of Embodiments 29-891, for manufacturing a medicament for preventing or treating a condition, disease or disorder.

953. Use of an oligonucleotide or composition of any one of Embodiments 29-891, for a method of any

one of Embodiments 22-28 and 892-947.

954. Use of an oligonucleotide or composition of any one of Embodiments 29-891, for manufacturing a medicament for a method of any one of Embodiments 22-28 and 892-947.

955. An oligonucleotide or composition of any one of Embodiments 29-891, for preventing or treating a condition, disease or disorder.

956. An oligonucleotide or composition of any one of Embodiments 29-891, for manufacturing a medicament for preventing or treating a condition, disease or disorder.

957. An oligonucleotide or composition of any one of Embodiments 29-891, for use in a method of any one of Embodiments 22-28 and 892-947.

958. An oligonucleotide or composition of any one of Embodiments 29-891, for use in manufacturing a medicament for a method of any one of Embodiments 22-28 and 892-947.

EXEMPLIFICATION

[01121] Certain examples of provided technologies (compounds (oligonucleotides, reagents, etc.), compositions, methods (methods of preparation, use, assessment, etc.), etc.) were presented herein. Those skilled in the art appreciate that many technologies, e.g., those described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO 2021/071858, WO 2022/099159, etc., can be utilized to prepare and/or assess properties and/or activities of provided technologies in accordance with the present disclosure.

Example 1. Useful technologies for assessing adenosine editing.

[01122] Oligonucleotide designs may be assessed using various systems. In some embodiments, oligonucleotides may be assessed and confirmed to provide editing in various cells. In some embodiments, oligonucleotides may be prepared and assessed in primary human hepatocytes (e.g., wild-type hepatocytes, I148M hepatocytes, etc.).

[01123] In some embodiments, oligonucleotide and compositions may be assessed and confirmed to provide editing in subjects. In some embodiments, oligonucleotides and compositions may be assessed and confirmed to provide editing in animals, e.g., mice, non-human primates (e.g., cynomolgus macaques), etc. In some embodiments, animals are transgenic animals, e.g., mice expressing human ADAR1. In some embodiments, animals are model animals comprising target adenosines associated with conditions, disorders or diseases. In some embodiments, provided technologies may efficient editing with or without exogenous ADAR polypeptides. In some embodiments, provided technologies may provide efficient editing without exogenous ADAR1 or ADAR2. In some embodiments, oligonucleotides and compositions may be delivered by transfection (e.g., using transfection compositions such as Lipofectamine RNAimax). In some embodiments, oligonucleotides and compositions may be delivered by gymnotic free update. Among other

things, the present disclosure provides technologies for assessing agents, e.g., oligonucleotides, and compositions thereof, for editing, e.g., A to I (G) editing. In some embodiments, the present disclosure provides technologies that are useful for assessing agents (e.g., oligonucleotides) and compositions thereof that interact with, and/or modulate or utilize one or more functions of an ADAR polypeptide as described herein, e.g., an ADAR1 polypeptide.

[01124] In some embodiments, the present disclosure provides non-human animal cells and/or non-human animals engineered to comprise and/or express an ADAR1 polypeptide or a characteristic portion thereof, or polynucleotide encoding an ADAR1 polypeptide or a characteristic portion thereof. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises a primate ADAR1 or a characteristic portion thereof. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises a primate ADAR1. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is a primate ADAR1. In some embodiments, a primate is a non-human primate. In some embodiments, a primate is human. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises human p110 ADAR1 or a characteristic portion thereof. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises human p110 ADAR1. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is human p110 ADAR1. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises human p150 ADAR1 or a characteristic portion thereof. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is or comprises human p150 ADAR1. In some embodiments, an ADAR1 polypeptide or a characteristic portion thereof is human p150 ADAR1. In some embodiments, a non-human animal is a rodent. In some embodiments, it is a rat. In some embodiments, it is a mouse. In some embodiments, the present disclosure provides mouse engineered to express human ADAR1. In some embodiments, the present disclosure provides mouse cells engineered to express human ADAR1.

[01125] Among other things, the present Example demonstrates that provided technologies are particularly useful for assessing agents, e.g., oligonucleotides, and compositions thereof that are useful for editing, e.g., adenosine editing described in the Examples. Among other things, the present disclosure provides that various agents (e.g., oligonucleotides) and compositions thereof that can provide editing in various human cells may show no or much lower levels of editing in certain cells (e.g., mouse cells) and certain animals such as rodents (e.g., mice) that do not contain or express human ADAR, e.g., human ADAR1; particularly, mice, a commonly used animal model, may be of limited uses for assessing various agents (e.g., oligonucleotides) for editing in humans, as agents active in human may show no or very low levels of activity. In some embodiments, the present disclosure provides cells and non-human animals (e.g., rodents such as mice) engineered to express human ADAR1 (e.g., human ADAR1 p110, p150, etc.), and their uses for assessing editing agents such as oligonucleotides and compositions thereof. Among other things, such engineered cells and/or animals can demonstrate activities that are more correlated with and/or predictive of activities in human cells than cells and/or animals not so engineered.

[01126] Generation of non-human mice expressing human ADAR1: Various technologies can be utilized in accordance with the present disclosure to provide mice engineered to express human ADAR1 polypeptide or a characteristic portion thereof. Certain useful technologies are described in the present disclosure and the priority applications, WO 2021/071858, WO 2022/046667, or WO 2022/099159.

[01127] Oligonucleotides and compositions can be delivered utilizing many technologies in accordance with the present disclosure. For example, in some embodiments, they may be delivered by transfection. In some embodiments, they may be delivered by gymnotic uptake. In some embodiments, oligonucleotides comprise moieties that can facilitate delivery. For example, in some embodiments, a moiety is a ligand for a polypeptide, e.g., a receptor, in many instances, on cell surface. In some embodiments, a polypeptide is expressed at a higher level by a type or population of cells, a tissue, etc. so that it may be utilized for delivery. In some embodiments, a ligand is an ASGPR ligand. In some embodiments, a ligand is or comprises GalNAc or a derivative thereof. In some embodiments, an oligonucleotide may comprise two or more ligand moieties, each of which is independently a ligand of a polypeptide. In some embodiments, an oligonucleotide comprises two or more copies of a ligand moiety. In some embodiments, a moiety targets one or more characteristics (e.g., pH, redox, etc.) of a location or environment.

[01128] In some embodiments, oligonucleotides and compositions can be administered to a system (e.g., cell line) and assessed for editing and activity of functional protein (e.g., functional protein encoded by a transcript comprising a target adenosine). In some embodiments, assessment of oligonucleotides and compositions can include a lipid droplet assay. In some embodiments, PNPLA3-I148M human primary hepatocytes were cultured in the BIOIVT Hepatopac system (BIOIVT Lot: KAN). Cultures were maintained in BIOIVT's Steatosis Application Media (BIOIVT, custommedia) without free fatty acids for 10 days and subsequently lipid loaded with 250uM Linoleic Acid (Thermo Scientific, AC215040250) for 4 days. After 24 hours in acclimatization media, 3uM Aimers (ADR-0110420, ADR-0110481, and ADR-0110482), 3uM non-targeting Aimer (ADR-0108273), 3uM siRNA (DSR-0105686), and mock (PBS) were repeat dosed every 96 hours. After 14 days, cultures were fixed with 4% Paraformaldehyde (Thermo Scientific, J61899. AK), permeabilized with 0.5% Triton-X100 (Thermo Scientific A16046.AE), blocked with 3% BSA (Fisher Scientific, BP9706100), stained with Bodipy 493/503 (Thermo Scientific, D3922), and DAPI (Thermo Scientific, EN62248). Imaging of the hepatocyte islands were completed on a fluorescence microscope with a 20x objective. Nuclei count and lipid droplet quantification was processed with FIJI-ImageJ.

[01129] In some embodiments, technologies of the provided technology can provide increased stability, high levels of editing, etc. In some embodiments, provided technologies can provide desired editing activities for a long period of time, e.g., about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45 or more days, after a last dose. In some embodiments, desired editing activities/levels of editing may be maintained for a long period of time, e.g., about or at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45 or more days, after a last dose.

[01130] In some embodiments, provided technologies can provide high levels of selectivity. In some

embodiments, about or at least about 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 95%, 96%, 97%, 98%, 99%, 99.5%, or 99.9% observed adenosine editing are at target adenosines. In some embodiments, about or at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% observed adenosine editing in coding regions are at target adenosines. In some embodiments, about or at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% observed adenosine editing in target nucleic acids (e.g., transcripts of target genes) are at target adenosines. In some embodiments, about or at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% observed adenosine editing in coding regions of target nucleic acids (e.g., transcripts of target genes) are at target adenosines. Various technologies, e.g., RNA-Seq, are available to those skilled in the art to assess selectivity; certain such technologies are described herein or in the priority applications, WO 2021/071858, WO 2022/046667, or WO 2022/099159. In some embodiments, a percentage for a selectivity described herein is at least about 80%. In some embodiments, it is at least about 85%. In some embodiments, it is at least about 90%. In some embodiments, it is at least about 95%. In some embodiments, it is at least about 96%. In some embodiments, it is at least about 97%. In some embodiments, it is at least about 98%. In some embodiments, it is at least about 99%. In some embodiments, it is at least about 99.5%. In some embodiments, it is at least about 99.9%. In some embodiments, it is about 100%. In some embodiments, no off-target editing is observed. In some embodiments, provided technology provides high selectivity *in vivo*.

[01131] In some embodiments, the present disclosure provides multiplex editing. In some embodiments, multiple target adenosines are edited together, one or more or each of which is independently edited at a comparable level compared to when edited individually.

[01132] Various results are presented in, e.g., Figures and Tables herein, as examples illustrating various benefits and advantages provided technologies can provide.

[01133] As demonstrated herein, the present disclosure among other things provide oligonucleotides comprising various modifications (e.g., nucleobase modifications, sugar modifications, linkage modifications, etc., and combinations and patterns thereof) that can provide efficient editing.

[01134] In some embodiments, utilization of certain sugars, e.g., natural DNA sugars, 2'-F modified sugars, etc. at and/or near editing sites provide editing activities. In some embodiments, an oligonucleotide comprises 5'-$N_1N_0N_{-1}$–3', wherein each of N_1, N_0, and N_{-1} is independently a nucleoside, N_1 and N_0 bond to an internucleotidic linkage as described herein, and N_{-1} and N_0 bond to an internucleotidic linkage as described herein, and N_0 is opposite to a target adenosine. In some embodiments, the sugar of each of N_1, N_0, and N_{-1} is independently a natural DNA sugar. In some embodiments, the sugar of N_1 is a 2'-modified sugar (e.g., a 2'-F modified sugar), and the sugar of each of N_0 and N_{-1} is independently a natural DNA sugar. In some embodiments, such oligonucleotides provide high editing levels. In some embodiments, 2'-OR modified sugars (wherein R is not –H) are utilized outside of a second subdomain or editing region, e.g., in a first domain, a first subdomain, and/or a third subdomain. Such modified sugars can be utilized at various positions in these domains/subdomains and are well tolerated and in various instances can improve properties and/or activities of oligonucleotides.

[01135] As demonstrated herein, provided technologies can provide efficient editing using significantly shorter oligonucleotides compared to various prior reported technologies. In some embodiments, oligonucleotides of various lengths, e.g., 27, 28, 29, 20, 31, 32, or more, nucleosides can provide editing.

[01136] In some embodiments, base sequences of oligonucleotides are of sufficient complementarity to those of target nucleic acids so that oligonucleotides can form duplexes under suitable conditions, e.g., *in vivo* or *in vitro* editing conditions. In some embodiments, oligonucleotides selectively form duplexes with target nucleic acids over non-target nucleic acids. While certain levels of complementarity to target nucleic acids are preferred or required for various uses including target adenosine editing, full complementarity is generally not required. In some embodiments, there are one or mismatches, bulges, etc. as described herein. In some embodiments, the nucleobase of a nucleoside opposite to target adenosine, N_0, is not complementary to a target adenosine. In some embodiments, hypoxanthine is utilized in place of G particularly if close or next to N_0. In some embodiments, first domains, first subdomains and/or third subdomains comprise one or more, e.g., 1, 2, 3, 4, or more, mismatches.

[01137] In some embodiments, oligonucleotides are provided in chirally controlled oligonucleotide compositions. In some embodiments, as illustrated herein, chirally controlled oligonucleotide compositions provide various desired properties and/or activities. In some embodiments, chirally controlled oligonucleotide compositions provide improved properties and/or activities compared to corresponding stereorandom oligonucleotide compositions (e.g., of oligonucleotides of the same constitution but not chirally controlled at chiral linkage phosphorus).

[01138] In some embodiments, an oligonucleotide is fully complementary to a sequence of the same length in a target nucleic acid. In some embodiments, an oligonucleotide is partially complementary to a sequence of the same length in a target nucleic acid.

[01139] Provided technologies can provide robust editing in the presence of ADAR1 and/or ADAR2. Provided technologies can provide robust editing in the presence of ADAR1-p110 and/or ADAR1-p150.

[01140] Data confirming various properties, activities, advantages, etc. of technologies of the present disclosure are provided as examples in various examples and figures including those in the priority applications, WO 2021/071858, WO 2022/046667, or WO 2022/099159. Certain useful technologies, e.g., structural elements, assays, targets, etc., that can be utilized in accordance with the present disclosure are described in WO 2021/071858 or WO 2022/099159.

Example 2. Preparation of oligonucleotide and compositions.

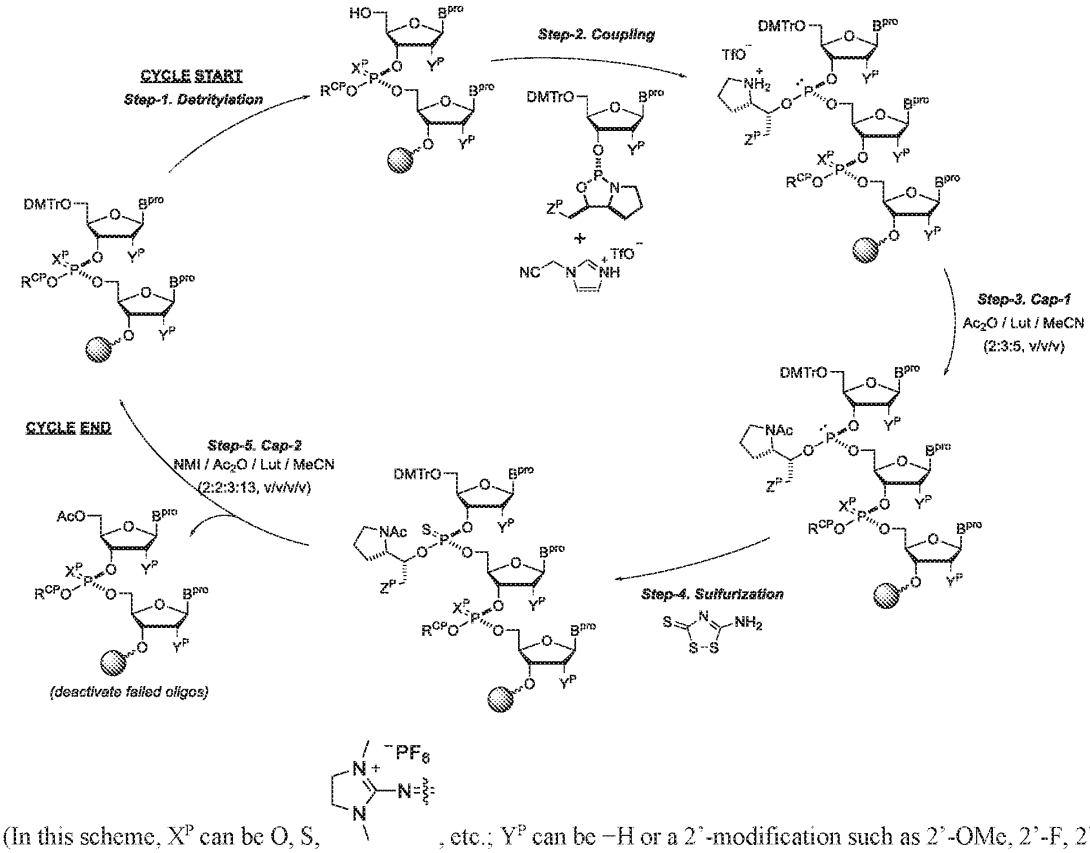
[01141] Various technologies for preparing oligonucleotides and oligonucleotide compositions (both stereorandom and chirally controlled) can be utilized in accordance with the present disclosure, including, for example, methods and reagents described in US 9982257, US 20170037399, US 20180216108, US 20180216107, US 9598458, WO 2017/062862, WO 2018/067973, WO 2017/160741, WO 2017/192679, WO 2017/210647, WO 2018/098264, WO 2018/223056, WO 2018/237194, WO 2019/032607, WO 2019/055951, WO 2019/075357, WO 2019/200185, WO 2019/217784, WO 2019/032612, WO 2020/191252, WO

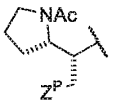
2021/071858, WO 2022/099159, and/or WO2023/201095, the methods and reagents of each of which are incorporated herein by reference. Many oligonucleotides and compositions thereof, were prepared and assessed and were confirmed to provide various activities, e.g., adenosine editing.

[01142] Certain useful cycles are described below as examples for preparing oligonucleotides.

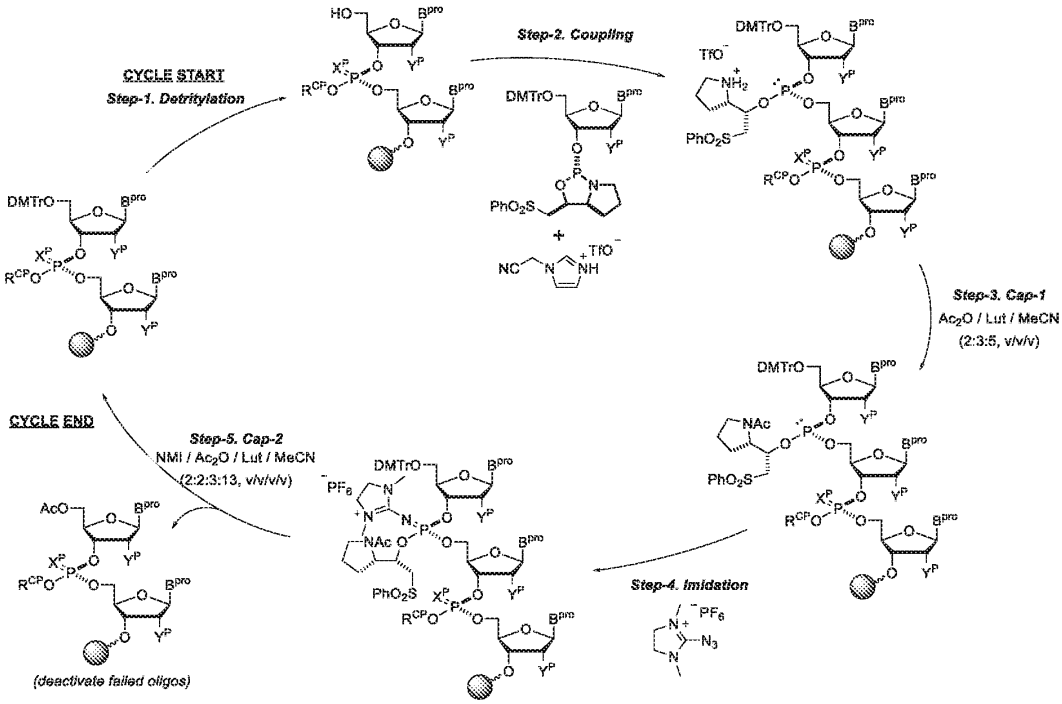
[01143] Among other things, these cycles are useful for preparing various oligonucleotides and compositions thereof, e.g., those described in Table 1 and Table 1A.

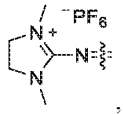
An example of a useful cycle for phosphorothioate assembly

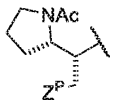


(In this scheme, X^P can be O, S, , etc.; Y^P can be −H or a 2'-modification such as 2'-OMe, 2'-F, 2'-MOE, etc.; Z^P can be $-SiPh_2Me$, $-SO_2Ph$, etc.; B^{pro} can be optionally protected nucleobases, e.g., A^{Bz}, G^{iBu}, C^{Ac}, U, etc.; R^{CP} can be a protecting group, e.g., $-CH_2CH_2CN$, , etc.).

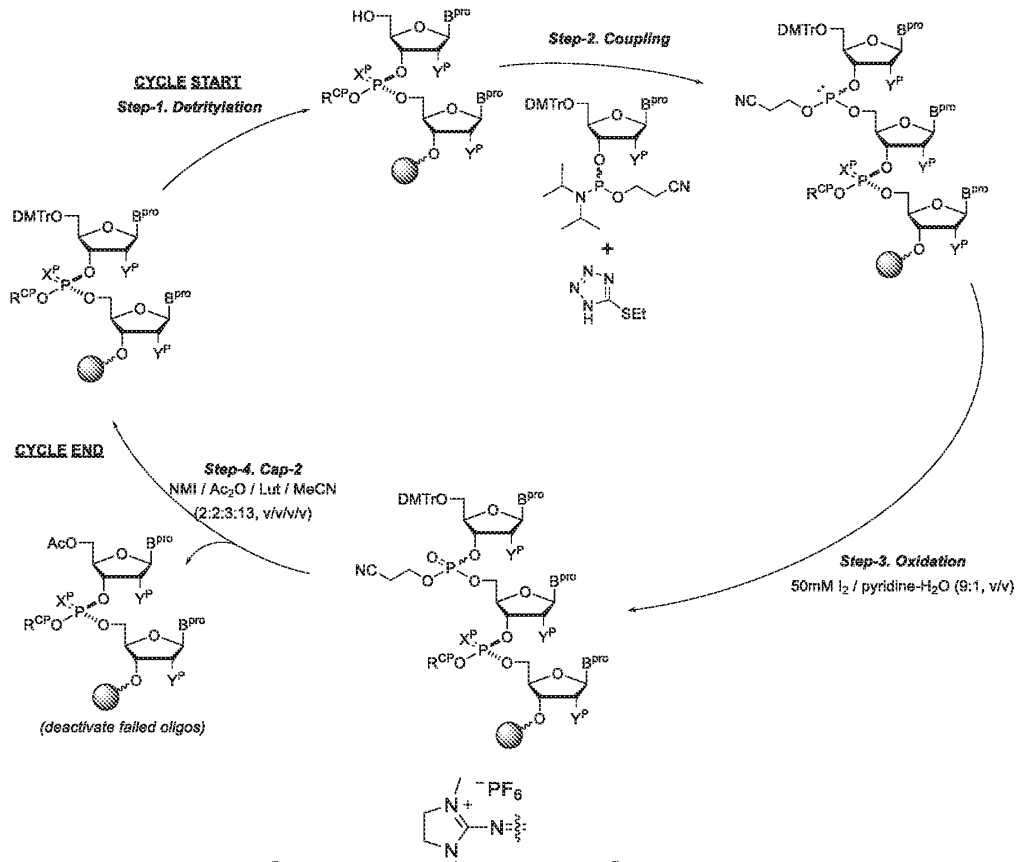
[01144] An example of a useful cycle for phosphoramidate assembly

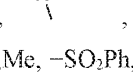
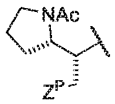




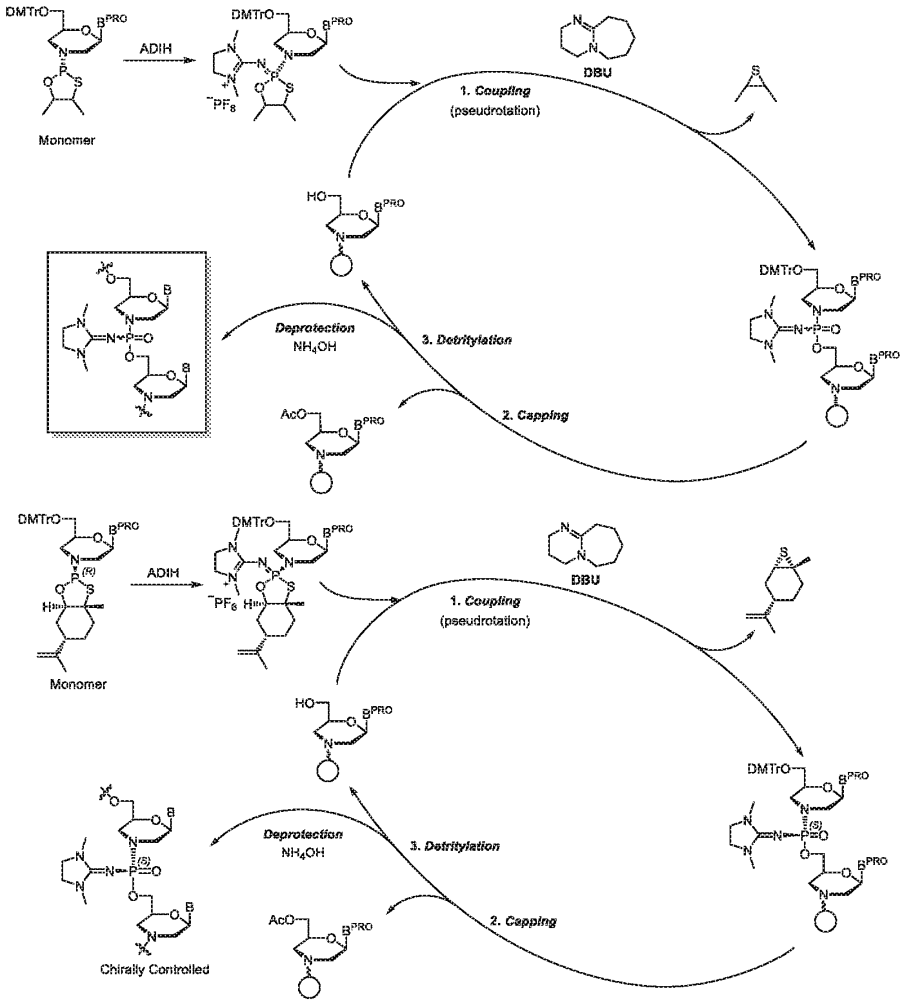
[01145] (In this scheme, X^P can be O, S, , etc.; Y^P can be –H or a 2'-modification such as 2'-OMe, 2'-F, 2'-MOE, etc.; B^{pro} can be optionally protected nucleobases, e.g., A^{Bz}, G^{iBu}, C^{Ac}, U, etc.; R^{CP} can be a protecting group, e.g., $-CH_2CH_2CN$, , etc.).

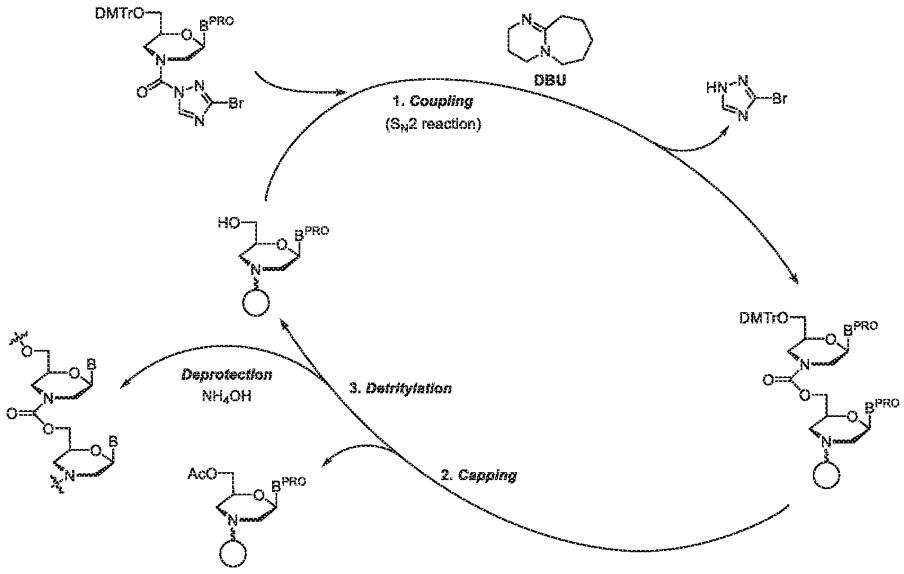
[01146] An example of a useful cycle for phosphate assembly



[01147] (In this scheme, X^P can be O, S, , etc.; Y^P can be −H or a 2'-modification such as 2'-OMe, 2'-F, 2'-MOE, etc.; Z^P can be $-SiPh_2Me$, $-SO_2Ph$, etc.; B^{pro} can be optionally protected nucleobases, e.g., A^{Bz}, G^{iBu}, C^{Ac}, U, etc.; R^{CP} can be a protecting group, e.g., $-CH_2CH_2CN$, , etc.).

[01148] Examples of other useful cycles


DMTrO
B^PRO
ADIH
Monomer
DBU
1. Coupling
(pseudrotation)
HO
Deprotection
NH4OH
3. Detritylation
2. Capping
AcO
Chirally Controlled



[01149] Each B is independently a nucleobase such as BA described herein (e.g., A, C, G, T, U, etc.). Each B^{PRO} is independently an optionally protected nucleobase such as BA described herein (e.g., A^{bz}, C^{ac}, G^{ibu}, T, U, etc. suitable for oligonucleotide synthesis). As shown, various linkages can be constructed to connect monomers to nucleosides or oligonucleotides including those on solid support. As appreciate by those skilled in the art these cycles can be utilized to couple monomers to −OH of various other types of sugars.

[01150] In some embodiments, preparations include one or more DPSE and/or PSM cycles.

[01151] A number of oligonucleotide compositions were synthesized and assessed, including, e.g., those in the Figures and Tables.

[01152] As described and confirmed herein, technologies of the present disclosure are useful for preparing various compositions of oligonucleotides comprising various structural features at various scales (e.g., 1 umol, 5 umol, 50 umol, etc.). It is understood that certain parameters will be modified based on the scale, e.g., volumes or equivalents. In some embodiments, as confirmed herein, provided technologies, e.g., those utilizing chiral auxiliaries comprising electron-withdrawing groups (e.g., R^{C1} comprising electron-withdrawing groups (e.g., $-SO_2R^{C1}$, $-C(O)R^{C1}$, etc.)) are particularly useful for preparing chirally controlled compositions of oligonucleotides comprising 2'-OH sugars (e.g., sugars with R^{2s} = OH, such as sugars typically found in natural RNA), particularly when such sugars are bonded to chirally controlled internucleotidic linkages.

Example 3. Example procedures for preparation of oligonucleotide compositions.

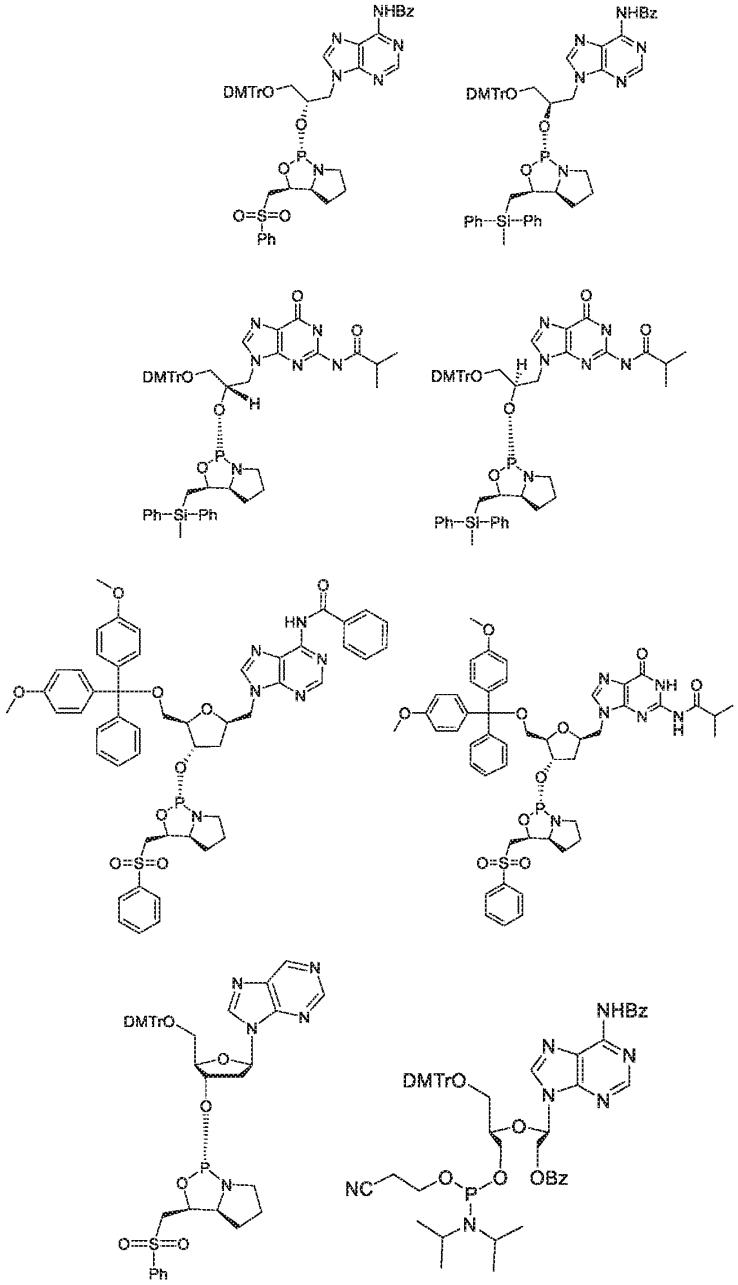
[01153] Certain stereopure oligonucleotides were synthesized at 1 umol scale using a MerMade192 synthesizer and universal CPG. In some embodiments, an amidite approach was used to incorporate GalNAc on the 5' end. In one preparation, generally, cyanoethyl amidites were used to prepare phosphate PO linkages, DPSE amidites for phosphorothioate PS linkages and PSM amidites for PN linkages. A typical MerMade192,

1 umol cycle is outlined in the table below:

Step	Operation	Reagents and Solvent	Volume	Approx. Total Time
1	Detritylation	3% dichloroacetic acid in toluene	5 x 225 uL	6.5 min
2	Double Coupling	0.1M phosphoramidite in combinations of ACN/IBN/PC/DMF and 0.5M CMIMT in ACN	95 uL / 110 uL (per coupling)	6 min (per coupling)
3	Cap 1	80% THF / 10% 2,6-lutidine / 10% acetic anhydride	200 uL	1.5 min
4	Oxidation (PO)	0.02M iodine in 70% THF / 20% pyridine / 10% water	200uL	1.5 min
	Sulfurization (PS)	0.1M xanthane hydride in 50% pyridine / 50% ACN	200 uL	6.5 min
	PN	0.3M ADIH in ACN	200 uL	7 min
5	Cap 2	80% THF / 10% 2,6-lutidine / 10% acetic anhydride and 16% n-methylimidazole in THF	100 uL / 100 uL	1.5 min

[01154] CMIMT: N-cyanomethylimidazolium triflate; ACN: acetonitrile; IBN: isobutyronitrile; ADIH: 2-azido-4,5-dihydro-1,3-dimethyl-1H-imidazolium hexafluorophosphate; THF: tetrahydrofuran; PC: propylene carbonate; DMF: dimethylformamide. The cycles were performed multiple times until the desired length was achieved.

[01155] Various useful phosphoramidites are reported and can be utilized in accordance with the present disclosure, e.g., those DPSE and PSM amidites with 2'-modifications and optionally protected nucleobases (see, e.g., US 20200231620, US 20230089442, etc.). For certain oligonucleotides, the following phosphoramidites were utilized:

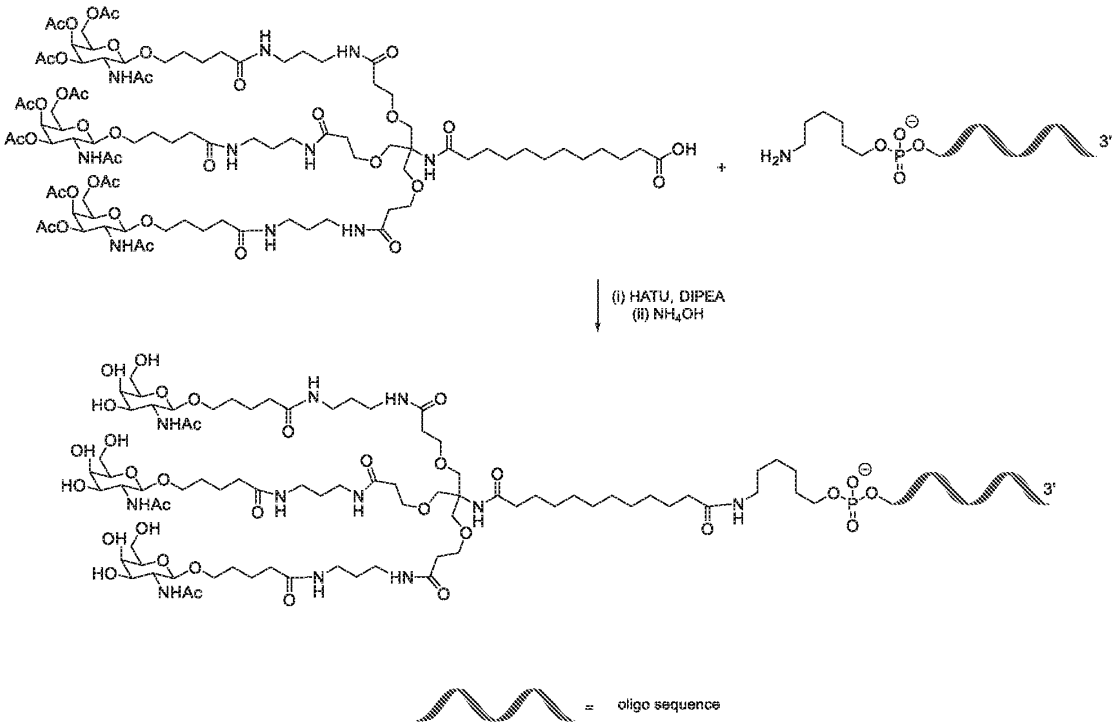


[01156] The first step of deprotection was performed on the synthesizer. 200 uL of 20% diethylamine in ACN was added to the column for 3 x 6 min followed by washing with ACN and drying. CPG was transferred to a container and 250 uL of fluoride solution was added. The fluoride solution consisted of dimethylformamide, water, triethylamine trihydrofluoride, and triethylamine (15.5/3.1/1.0/1.8 volume ratio). After about 4 hours at room temperature, approximately 375 uL of 30% ammonium hydroxide was added, and the reaction incubated at 37 °C overnight. The CPG was filtered and washed with water and the filtrate

collected.

[01157] The oligonucleotides were purified by anion exchange purification at room temperature. The oligonucleotide was loaded onto a column packed with Source Q15 resin after equilibration with a 20 mM sodium hydroxide in 20% acetonitrile mobile phase. The purified oligonucleotide was eluted using a mobile phase of 20 mM sodium hydroxide and 2.5 M sodium chloride in 20% acetonitrile. The desired fraction was desalted using a G-25 Sephadex column against water for injection. Desalted samples were dried, reconstituted and analyzed.

[01158] A useful protocol for GalNAc conjugation is described below as an example.



[01159] Additional chemical moieties can also be installed by coupling with phosphoramidites comprising such additional chemical moieties (and optional linkers), e.g., phosphoramidites comprising GalNAc such as those described in Examples below. Additional technologies for preparing oligonucleotides are illustrated below as examples.

[01160] Among other things, technologies described in this Example can be utilized to prepare various oligonucleotide compositions in Table 1 and Table 1A.

Example 4. Example procedure for preparation of oligonucleotide compositions.

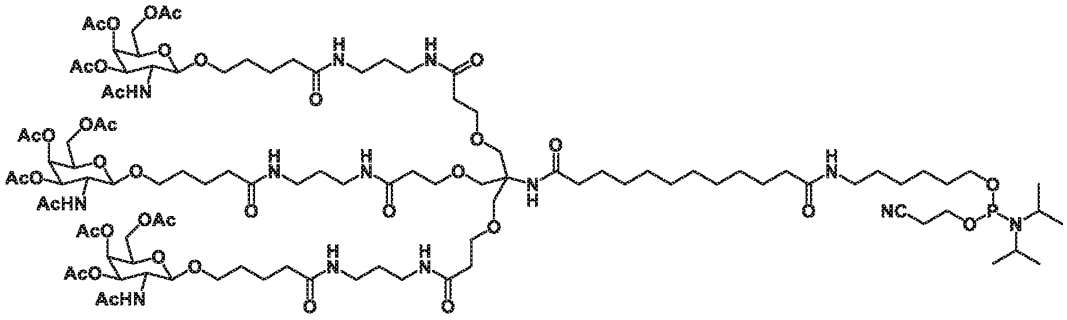
[01161] Certain stereopure oligonucleotides were synthesized at 50 umol scale using a MerMade12 synthesizer and standard CPG. In some embodiments, an amidite approach was used to incorporate GalNAc on the 5' end. In one preparation, generally, cyanoethyl amidites were used to prepare phosphate PO linkages,

DPSE amidites for phosphorothioate PS linkages and PSM amidites for PN linkages. A typical MerMade12, 50 umol cycle is outlined in the table below:

Step	Operation	Reagents and Solvent	Volume	Approx. Total Time
1	Detritylation	3% dichloroacetic acid in toluene	4 x 4.5 mL	5 min
2	Single Coupling	0.15M phosphoramidite in combinations of ACN/IBN/PC and 0.5M CMIMT in ACN	15 mL / 2.25 mL	6-12 min
3	Cap 1	80% THF / 10% 2,6-lutidine / 10% acetic anhydride	5 mL	1 min
4	Oxidation (PO)	0.02M iodine in 70% THF / 20% pyridine / 10% water	6 mL	2-4 min
	Sulfurization (PS)	0.1M xanthane hydride in 50% pyridine / 50% ACN	6 mL	6 min
	PN	0.3M ADIH in ACN	6 mL	10 min
5	Cap 2	80% THF / 10% 2,6-lutidine / 10% acetic anhydride and 16% n-methylimidazole in THF	2.5 mL / 2.5 mL	1min

[01162] CMIMT: N-cyanomethylimidazolium triflate; ACN: acetonitrile; IBN: isobutyronitrile; ADIH: 2-azido-4,5-dihydro-1,3-dimethyl-1H-imidazolium hexafluorophosphate; THF: tetrahydrofuran; PC: propylene carbonate. The cycles were performed multiple times until the desired length was achieved.

[01163] In some embodiments, an amidite approach was used to incorporate GalNAc on the 5' end using the phosphoramidite below. See, e.g., WO 2023201095.



[01164] The GalNAc amidite was coupled either as a single 10-15 min or a two x 10 min procedure. For each coupling, 1.5 mL of 0.2 M GalNAc amidite and 3 mL of CMIMT in ACN were added.

[01165] The first step of deprotection was performed on the synthesizer. 6 mL of 20% diethylamine in ACN was added to the column for 10 min followed by washing with ACN and drying. CPG was transferred to a tube and 5 mL of fluoride solution was added. The fluoride solution consisted of dimethylsulfoxide, water, triethylamine trihydrofluoride, and triethylamine (15.5/3.1/1.0/1.8 volume ratio). After about 1 hour at room temperature, approximately 10 mL of 30% ammonium hydroxide was added, and the reaction incubated at 37

°C overnight. The CPG was filtered off and washed with water and the filtrate collected.

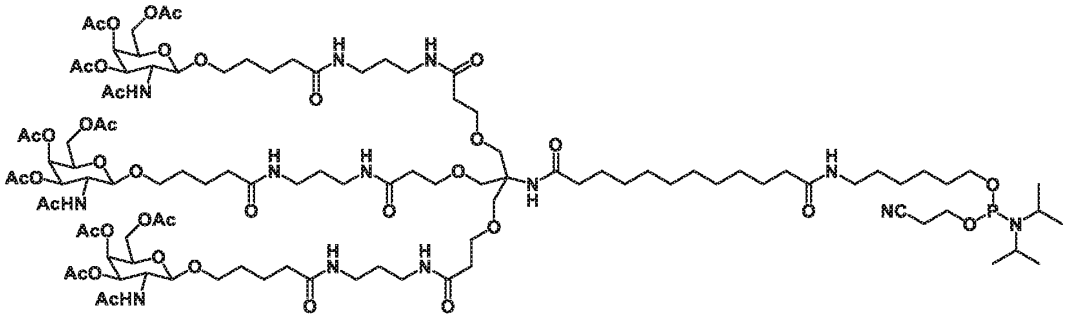
[01166] The oligonucleotides were purified by anion exchange purification at room temperature. The oligonucleotide was loaded onto a column packed with Source Q15 resin after equilibration with a 20 mM sodium hydroxide in water or 20 mM sodium hydroxide with 20% acetonitrile in water mobile phase. The purified oligonucleotide was eluted as fractions by gradient elution with a mobile phase of 20 mM sodium hydroxide and 2.5 M sodium chloride in water or 20 mM sodium hydroxide and 2.5 M sodium chloride with 20% acetonitrile in water. Fractions were analyzed, pooled to the desired purity and desalted using a G-25 Sephadex column against water for injection. Desalted samples were dried, reconstituted and sterile filtered prior to final analysis including UPLC, LC-MS and UV-Vis.

[01167] Certain oligonucleotides were synthesized at 250 umol scale using a MerMade12 synthesizer and standard CPG. In some embodiments, an amidite approach was used to incorporate GalNAc on the 5' end. In one preparation, generally, cyanoethyl amidites were used to prepare phosphate PO linkages, DPSE amidites for phosphorothioate PS linkages and PSM amidites for PN linkages. A typical MerMade12, 250 umol cycle is outlined in the table below:

Step	Operation	Reagents and Solvent	Volume	Approx. Total Time
1	Detritylation CPG	3% dichloroacetic acid in toluene	5 x 20 mL	5 min
	Detritylation Base 2-end	3% dichloroacetic acid in toluene	4 x 20 mL	4 min
2	Single Coupling	0.15M phosphoramidite in combinations of ACN/IBN/PC and 0.5M CMIMT in ACN	7.5 mL / 11.7 mL	6-12 min
3	Cap 1	80% THF / 10% 2,6-lutidine / 10% acetic anhydride	20 mL	1 min
4	Oxidation (PO)	0.02M iodine in 70% THF / 20% pyridine / 10% water	19.2 mL	2-4 min
	Sulfurization (PS)	0.1M xanthane hydride in 50% pyridine / 50% ACN	19.2 mL	6 min
	PN	0.3M ADIH in ACN	19 mL	10 min
5	Cap 2	80% THF / 10% 2,6-lutidine / 10% acetic anhydride and 16% n-methylimidazole in THF	10 mL / 10 mL	1min

[01168] CMIMT: N-cyanomethylimidazolium triflate; ACN: acetonitrile; IBN: isobutyronitrile; ADIH: 2-azido-4,5-dihydro-1,3-dimethyl-1H-imidazolium hexafluorophosphate; THF: tetrahydrofuran; PC: propylene carbonate. The cycles were performed multiple times until the desired length was achieved.

[01169] In some embodiments, an amidite approach was used to incorporate GalNAc on the 5' end using the phosphoramidite below. See, e.g., WO 2023201095.



[01170] The GalNAc amidite was coupled either as a single 10-15 min or a two x 10 min procedure. For each coupling, 7.5 mL of 0.2 M GalNAc amidite and 15 mL of CMIMT in ACN were added.

[01171] The first step of deprotection was performed on the synthesizer. 23.3 mL of 20% diethylamine in ACN was added to the column for 10 min followed by washing with ACN and drying. CPG was transferred to a tube and 25 mL of fluoride solution was added. The fluoride solution consisted of dimethylsulfoxide, water, triethylamine trihydrofluoride, and triethylamine (15.5/3.1/1.0/1.8 volume ratio). After about 1 hour at room temperature, approximately 50 mL of 30% ammonium hydroxide was added, and the reaction incubated at 37 °C overnight. The CPG was filtered off and washed with water and the filtrate collected.

[01172] The oligonucleotides were purified by anion exchange purification at room temperature. The oligonucleotide was loaded onto a column packed with Source Q15 resin after equilibration with a 20 mM sodium hydroxide in water or 20 mM sodium hydroxide with 20% acetonitrile in water mobile phase. The purified oligonucleotide was eluted as fractions by gradient elution with a mobile phase of 20 mM sodium hydroxide and 2.5 M sodium chloride in water or 20 mM sodium hydroxide and 2.5 M sodium chloride with 20% acetonitrile in water. Fractions were analyzed, pooled to the desired purity and desalted using a G-25 Sephadex column against water for injection. Desalted samples were dried, reconstituted and sterile filtered prior to final analysis including UPLC, LC-MS and UV-Vis.

[01173] Among other things, technologies described in this Example can be utilized to prepare various oligonucleotide compositions in Table 1 and Table 1A. Certain data of prepared oligonucleotide compositions using technologies in Examples described herein or similar technologies are presented below in the Examples below.

Example 5. Provided technologies can provide editing.

[01174] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 1. Primary wild-type (WT) human hepatocytes were dosed with 5uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in I148 codon (i.e., AUC) of WT human PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e.,

GUC). At 48 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

Example 6. Provided technologies can provide editing.

[01175] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 2. Primary human hepatocytes homozygous for M148 mutation were dosed with 10 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 48 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

Example 7. Provided technologies can provide editing.

[01176] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), sugars (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 3. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.1 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 72 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

[01177] In some embodiments, oligonucleotides comprising a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine can provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine). In some embodiments, oligonucleotides comprising one or more PN internucleotidic linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a one or more PN linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13})). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_{16}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_{16}).

Example 8. Provided technologies can provide editing.

[01178] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), sugars (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 4. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.1 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 72 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

[01179] In some embodiments, oligonucleotides comprising a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine can provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine). In some embodiments, oligonucleotides comprising one or more PN internucleotidic linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a one or more PN linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13})). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9). In some embodiments, oligonucleotides comprising one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide)).

Example 9. Provided technologies can provide editing.

[01180] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), sugars (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 5 and Figure 6. Primary human hepatocytes homozygous for M148 mutation were dosed with 0.01 uM of indicated oligonucleotides. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 72 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

[01181] In some embodiments, oligonucleotides comprising a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine can provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine). In some embodiments, oligonucleotides comprising one or more PN internucleotidic linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a one or more PN linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13})). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9). In some embodiments, oligonucleotides comprising one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide)). In some embodiments, oligonucleotides comprising one or more 2'-OMe modifications (e.g., one or more 2'-OMe modifications at one or more of N_{11}, N_{12}, and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more 2'-OMe modifications (e.g., one or more 2'-OMe modifications at one or more of N_{11}, N_{12}, and N_{13})).

Example 10. Provided technologies can provide editing and produce functional protein.

[01182] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), sugars (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 7, Figure 8, and Figure 9. As shown in Figure 7, primary human hepatocytes were dosed with siRNA constructs targeting PNPLA3 at indicated concentration and PNPLA3 transcript levels were assessed. Cells were also treated with 250 uM of linoleic acid (LA) lipid and assessed for lipid droplet formation under the protocol outlined in Example 1 above. As shown in Figure 8, primary human hepatocytes homozygous for M148 mutation were dosed with 0.01 uM of indicated oligonucleotides. Cells were also treated with 250 uM of linoleic acid (LA) lipid and assessed for lipid droplet formation under the protocol outlined in Example 1 above. As shown in Figure 9, primary human hepatocytes homozygous for M148 mutation were dosed with indicated concentrations of indicated oligonucleotides. Cells were also treated with 250 uM of linoleic acid (LA) lipid and assessed for lipid droplet formation under the protocol outlined in Example 1 above. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 72 hours following oligonucleotide

addition, cells were harvested and RNA collected (Figure 9). RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

[01183] In some embodiments, oligonucleotides comprising a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine can provide editing levels sufficient to produce comparable or increased levels of functional protein (e.g., PNPLA3) as compared to a reference (e.g., siRNA construct, no treatment control, etc.). In some embodiments, oligonucleotides comprising one or more PN internucleotidic linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13}) may provide editing levels sufficient to produce comparable or increased levels of functional protein (e.g., PNPLA3) as compared to a reference (e.g., siRNA construct, no treatment control, etc.). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9) provide editing levels sufficient to produce comparable or increased levels of functional protein (e.g., PNPLA3) as compared to a reference (e.g., siRNA construct, no treatment control, etc.). In some embodiments, oligonucleotides comprising one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide) may provide editing levels sufficient to produce comparable or increased levels of functional protein (e.g., PNPLA3) as compared to a reference (e.g., siRNA construct, no treatment control, etc.). In some embodiments, oligonucleotides comprising one or more 2'-OMe modifications (e.g., one or more 2'-OMe modifications at one or more of N_{11}, N_{12}, and N_{13}) may provide editing levels sufficient to produce comparable or increased levels of functional protein (e.g., PNPLA3) as compared to a reference (e.g., siRNA construct, no treatment control, etc.).

Example 11. Mass spectrometry of certain provided oligonucleotides.

[01184] Oligonucleotides comprising various modifications, such as base modifications (e.g., [3nU]), linkage modifications (e.g., PS, PN (e.g., phosphoryl guanidine linkages such as n001), etc.), sugar modifications (e.g., 2'-F, 2'-OMe, 2'-MOE, etc.), and stereochemistry and patterns thereof were designed, manufactured, characterized and assessed. For example, certain mass spectrometry data are presented below, confirming that oligonucleotides comprising various modifications, stereochemistry and patterns thereof were made. Mass spectrometry was performed on a Novatia Oligo HTCS instrument. Certain data (molecular weight (Da) and observed mass (Da)) are presented in the table below.

Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0110736	12650.38	12647.4	ADR-0110420	12668.37	12666
ADR-0110722	12650.38	12647.4	ADR-0110894	12524.25	12522.1
ADR-0110721	12650.38	12647.4	ADR-0110915	12714.53	12712.4
ADR-0110922	12690.47	12687.5	ADR-0110912	12785.62	12783.5
ADR-0110773	12656.34	12653.4	ADR-0110719	12664.41	12662.3
ADR-0110871	12690.4	12687.5	ADR-0110726	12664.41	12662.3
ADR-0110869	12690.4	12687.5	ADR-0110928	12690.47	12688.4
ADR-0110734	12650.38	12647.5	ADR-0110927	12690.47	12688.4
ADR-0110735	12650.38	12647.5	ADR-0110772	13027.67	13025.6
ADR-0110730	12650.38	12647.5	ADR-0110908	12607.37	12605.3

ADR-0110929	12690.47	12687.6	ADR-0110891	12615.36	12613.3
ADR-0110904	12690.4	12687.6	ADR-0110921	12706.54	12704.5
ADR-0110732	12650.38	12647.6	ADR-0110690	12664.33	12662.3
ADR-0110723	12650.38	12647.6	ADR-0110687	12664.33	12662.3
ADR-0110646	12721.58	12718.8	ADR-0110374	12570.43	12568.4
ADR-0110729	12650.38	12647.7	ADR-0110692	12664.33	12662.3
ADR-0110896	12781.51	12778.9	ADR-0110697	12664.33	12662.3
ADR-0110914	12781.58	12779	ADR-0110868	12682.32	12680.3
ADR-0110724	12650.38	12647.8	ADR-0110882	12690.4	12688.4
ADR-0110888	12607.37	12604.8	ADR-0110714	12680.4	12678.4
ADR-0110749	12646.42	12643.9	ADR-0110934	12761.47	12759.5
ADR-0110887	12607.37	12604.9	ADR-0110369	12524.34	12522.4
ADR-0110731	12650.38	12648	ADR-0110686	12664.33	12662.4
ADR-0110733	12650.38	12648	ADR-0110691	12664.33	12662.4
ADR-0110775	12589.29	12587.4	ADR-0110770	12653.36	12651.8
ADR-0110905	12698.48	12696.6	ADR-0109986	12552.44	12554
ADR-0110890	12615.36	12613.5	ADR-0110900	12694.44	12692.9
ADR-0110870	12690.4	12688.6	ADR-0110878	12694.44	12692.9
ADR-0110889	12607.28	12605.5	ADR-0110392	12570.43	12568.9
ADR-0110895	12524.25	12522.5	ADR-0110689	12664.33	12662.8
ADR-0110762	12747.45	12745.7	ADR-0110378	12556.41	12554.9
ADR-0110932	12777.54	12775.8	ADR-0109982	12556.41	12554.9
ADR-0110647	12717.63	12715.9	ADR-0110688	12652.3	12650.8
ADR-0110910	12785.62	12783.9	ADR-0110738	12594.29	12592.8
ADR-0110740	12646.42	12644.7	ADR-0110753	12632.39	12630.9
ADR-0109971	12540.41	12538.7	ADR-0110873	12599.29	12597.8
ADR-0110909	12793.61	12791.9	ADR-0110906	12698.48	12697
ADR-0110886	12607.37	12605.7	ADR-0110771	12678.38	12676.9
ADR-0110892	12615.36	12613.7	ADR-0109990	12552.44	12553.9
ADR-0110742	12620.36	12618.7	ADR-0110407	12636.34	12637.8
ADR-0110397	12524.34	12522.7	ADR-0110893	12524.25	12522.8
ADR-0110876	12694.44	12692.8	ADR-0110649	12663.54	12662.1
ADR-0110923	12706.54	12704.9	ADR-0110739	12594.29	12592.9
ADR-0110648	12649.51	12647.9	ADR-0110750	12632.39	12631
ADR-0110713	12680.4	12678.8	ADR-0110874	12599.29	12597.9
ADR-0110702	12680.4	12678.8	ADR-0110641	12721.58	12720.2
ADR-0110709	12680.4	12678.8	ADR-0108504	12332.14	12333.5
Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0110639	12635.49	12633.9	ADR-0109984	12552.44	12553.8
ADR-0110754	12632.39	12630.8	ADR-0110402	12640.38	12639.4
ADR-0110899	12694.44	12693.1	ADR-0110884	12698.48	12697.5
ADR-0110898	12694.44	12693.1	ADR-0108485	12458.12	12459.1
ADR-0110399	12540.34	12539	ADR-0110867	12777.47	12776.5
ADR-0110877	12694.44	12693.1	ADR-0109989	12552.44	12553.4
ADR-0110396	12540.41	12539.1	ADR-0108506	12332.14	12333.1
ADR-0110398	12556.41	12555.1	ADR-0109998	12552.44	12553.4
ADR-0110460	12557.4	12556.1	ADR-0108518	13050.74	13049.8
ADR-0108499	12293.1	12294.4	ADR-0110475	12630.49	12631.4
ADR-0109992	12552.44	12553.7	ADR-0110418	12798.61	12797.7
ADR-0109994	12552.44	12553.7	ADR-0110645	12637.5	12636.6

ADR-0109996	12552.44	12553.7	ADR-0108501	12293.1	12294
ADR-0110875	12686.36	12685.1	ADR-0110372	12614.49	12613.6
ADR-0109987	12552.44	12553.7	ADR-0109972	12528.38	12527.5
ADR-0109999	12552.44	12553.7	ADR-0110491	12925.63	12926.5
ADR-0109985	12552.44	12553.7	ADR-0110519	12623.37	12622.5
ADR-0109991	12552.44	12553.7	ADR-0108514	12333.13	12334
ADR-0110666	12765.45	12764.2	ADR-0108492	12442.14	12443
ADR-0110424	12747.45	12746.2	ADR-0110049	12594.46	12593.6
ADR-0110925	12686.43	12685.2	ADR-0108505	12332.14	12333
ADR-0108483	12312.17	12313.4	ADR-0110760	12747.45	12746.6
ADR-0108497	12276.11	12274.9	ADR-0110757	12747.45	12746.6
ADR-0110370	12538.4	12537.2	ADR-0110913	12769.55	12768.7
ADR-0110931	12702.5	12701.3	ADR-0110759	12747.45	12746.6
ADR-0110706	12680.4	12679.2	ADR-0110881	12603.33	12602.5
ADR-0110920	12702.5	12701.3	ADR-0110879	12603.33	12602.5
ADR-0110748	12634.39	12633.2	ADR-0110678	12743.41	12742.6
ADR-0110747	12634.39	12633.2	ADR-0110410	12814.61	12813.8
ADR-0110907	12698.48	12697.3	ADR-0110430	12743.41	12742.6
ADR-0110926	12698.46	12697.3	ADR-0110755	12632.39	12631.6
ADR-0110897	12686.36	12685.2	ADR-0110745	12632.39	12631.6
ADR-0108512	12332.14	12333.3	ADR-0110657	12830.48	12829.7
ADR-0110391	12538.36	12537.2	ADR-0109976	12528.38	12527.6
ADR-0110406	12719.46	12718.3	ADR-0110675	12826.44	12827.2
ADR-0110408	12719.46	12718.3	ADR-0110004	12524.34	12525.1
ADR-0110435	12727.41	12728.5	ADR-0110454	12726.56	12725.8
ADR-0110883	12698.48	12697.4	ADR-0110651	12765.45	12764.7
ADR-0110885	12698.48	12697.4	ADR-0110758	12747.45	12746.7
ADR-0109997	12552.44	12553.5	ADR-0110488	12931.66	12932.4
ADR-0109988	12552.44	12553.5	ADR-0110918	12706.54	12705.8
ADR-0109993	12552.44	12553.5	ADR-0110411	12798.54	12797.8
ADR-0109995	12552.44	12553.5	ADR-0110434	12810.53	12809.8
ADR-0109983	12552.44	12553.5	ADR-0110746	12646.42	12645.7
ADR-0108507	12332.14	12333.2	ADR-0110395	12509.32	12508.3
ADR-0110756	12747.45	12746.4	ADR-0110643	12649.51	12648.5
ADR-0110933	12777.54	12776.5	ADR-0110373	12598.42	12597.7
Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0110737	12520.21	12519.5	ADR-0110679	12676.36	12676.9
ADR-0110667	12751.4	12752.1	ADR-0110495	13045.76	13046.3
ADR-0110382	12482.3	12483	ADR-0110916	12706.54	12706
ADR-0110466	12557.4	12558.1	ADR-0110008	12524.34	12523.8
ADR-0110705	12680.4	12679.7	ADR-0110482	12755.44	12754.9
ADR-0110711	12680.4	12679.7	ADR-0110695	12664.33	12663.8
ADR-0110701	12680.4	12679.7	ADR-0110901	12603.33	12602.8
ADR-0110774	12589.29	12588.6	ADR-0110902	12603.33	12602.8
ADR-0110751	12632.39	12631.7	ADR-0110486	12771.42	12770.9
ADR-0110743	12632.39	12631.7	ADR-0110522	12627.32	12626.8
ADR-0110672	12830.48	12829.8	ADR-0110496	13089.82	13089.3
ADR-0110427	12759.48	12758.8	ADR-0110027	12619.49	12620
ADR-0108487	12724.48	12723.8	ADR-0110669	12751.4	12751.9
ADR-0110494	12929.58	12928.9	ADR-0110670	12751.4	12751.9

ADR-0109974	12461.33	12462	ADR-0110716	12680.4	12679.9
ADR-0110453	12627.37	12626.7	ADR-0110707	12680.4	12679.9
ADR-0109975	12461.33	12462	ADR-0110708	12680.4	12679.9
ADR-0110673	12826.44	12827.1	ADR-0110371	12558.4	12557.9
ADR-0108509	12364.14	12364.8	ADR-0110467	12572.41	12572.9
ADR-0110741	12620.36	12619.7	ADR-0110458	12572.41	12572.9
ADR-0110480	12568.35	12567.7	ADR-0110465	12572.41	12572.9
ADR-0110445	12659.44	12658.8	ADR-0110464	12572.41	12572.9
ADR-0110376	12568.42	12567.8	ADR-0110473	12566.42	12566.9
ADR-0110663	12743.41	12742.8	ADR-0110385	12514.37	12513.9
ADR-0110443	12564.29	12564.9	ADR-0110390	12554.43	12554.9
ADR-0110671	12751.4	12752	ADR-0110055	12580.43	12580.9
ADR-0110710	12680.4	12679.8	ADR-0110525	12781.53	12782
ADR-0110421	12680.4	12679.8	ADR-0110052	12580.43	12580.9
ADR-0110712	12680.4	12679.8	ADR-0110045	12580.43	12580.9
ADR-0110042	12568.4	12567.8	ADR-0110051	12580.43	12580.9
ADR-0110717	12680.4	12679.8	ADR-0108508	12348.14	12348.6
ADR-0110456	12572.41	12573	ADR-0110415	12703.46	12703
ADR-0110469	12572.41	12573	ADR-0110043	12594.46	12594
ADR-0110704	12624.31	12624.9	ADR-0110768	12747.45	12747
ADR-0110461	12572.41	12573	ADR-0110769	12747.45	12747
ADR-0108495	12351.21	12351.8	ADR-0110426	12747.45	12747
ADR-0110457	12572.41	12573	ADR-0110765	12747.45	12747
ADR-0110744	12632.39	12631.8	ADR-0110767	12747.45	12747
ADR-0109973	12528.38	12527.8	ADR-0110414	12620.34	12619.9
ADR-0110437	12743.48	12742.9	ADR-0108478	12352.23	12351.8
ADR-0110677	12834.43	12835	ADR-0110438	12568.33	12567.9
ADR-0110429	12826.53	12827.1	ADR-0110903	12603.33	12602.9
ADR-0110384	12514.37	12513.8	ADR-0110880	12603.33	12602.9
ADR-0110057	12594.46	12593.9	ADR-0108481	12510.39	12510.8
ADR-0110660	12826.44	12827	ADR-0108479	12510.39	12510.8
ADR-0110416	12782.54	12783.1	ADR-0108498	12276.11	12275.7
ADR-0110431	12731.45	12730.9	ADR-0110684	11258.3	11257.9
Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0110679	12676.36	12676.9	ADR-0110470	12557.4	12557.8
ADR-0110495	13045.76	13046.3	ADR-0110523	12769.5	12769.9
ADR-0110916	12706.54	12706	ADR-0110048	12568.4	12568
ADR-0110008	12524.34	12523.8	ADR-0110653	12751.4	12751.8
ADR-0110482	12755.44	12754.9	ADR-0108500	12293.1	12293.5
ADR-0110695	12664.33	12663.8	ADR-0108503	12293.1	12293.5
ADR-0110901	12603.33	12602.8	ADR-0110524	12769.5	12769.9
ADR-0110902	12603.33	12602.8	ADR-0110034	12619.49	12619.1
ADR-0110486	12771.42	12770.9	ADR-0110463	12572.41	12572.8
ADR-0110522	12627.32	12626.8	ADR-0110447	12726.49	12726.1
ADR-0110496	13089.82	13089.3	ADR-0110046	12515.38	12515
ADR-0110027	12619.49	12620	ADR-0108491	12506.42	12506.8
ADR-0110669	12751.4	12751.9	ADR-0110380	12498.37	12498
ADR-0110670	12751.4	12751.9	ADR-0110694	12664.33	12664.7
ADR-0110716	12680.4	12679.9	ADR-0110484	12763.43	12763.8
ADR-0110707	12680.4	12679.9	ADR-0110425	12664.33	12664.7

ADR-0110708	12680.4	12679.9	ADR-0110674	12826.44	12826.8
ADR-0110371	12558.4	12557.9	ADR-0110439	12580.36	12580
ADR-0110467	12572.41	12572.9	ADR-0110763	12747.45	12747.1
ADR-0110458	12572.41	12572.9	ADR-0109978	12640.45	12640.1
ADR-0110465	12572.41	12572.9	ADR-0110766	12747.45	12747.1
ADR-0110464	12572.41	12572.9	ADR-0108494	12328.17	12328.5
ADR-0110473	12566.42	12566.9	ADR-0110000	12536.37	12536.7
ADR-0110385	12514.37	12513.9	ADR-0110001	12536.37	12536.7
ADR-0110390	12554.43	12554.9	ADR-0110017	12536.37	12536.7
ADR-0110055	12580.43	12580.9	ADR-0110013	12536.37	12536.7
ADR-0110525	12781.53	12782	ADR-0110014	12536.37	12536.7
ADR-0110052	12580.43	12580.9	ADR-0110016	12536.37	12536.7
ADR-0110045	12580.43	12580.9	ADR-0110003	12536.37	12536.7
ADR-0110051	12580.43	12580.9	ADR-0108484	12446.18	12446.5
ADR-0108508	12348.14	12348.6	ADR-0110720	12650.38	12650.7
ADR-0110415	12703.46	12703	ADR-0110403	12652.41	12652.1
ADR-0110043	12594.46	12594	ADR-0110037	12619.49	12619.8
ADR-0110768	12747.45	12747	ADR-0110022	12619.49	12619.8
ADR-0110769	12747.45	12747	ADR-0110442	12647.41	12647.1
ADR-0110426	12747.45	12747	ADR-0110383	12482.3	12482.6
ADR-0110765	12747.45	12747	ADR-0110487	12887.6	12887.3
ADR-0110767	12747.45	12747	ADR-0110703	12680.4	12680.1
ADR-0110414	12620.34	12619.9	ADR-0110656	12751.4	12751.7
ADR-0108478	12352.23	12351.8	ADR-0110718	12680.4	12680.1
ADR-0110438	12568.33	12567.9	ADR-0110640	12637.5	12637.8
ADR-0110903	12603.33	12602.9	ADR-0110655	12751.4	12751.7
ADR-0110880	12603.33	12602.9	ADR-0110474	12574.4	12574.7
ADR-0108481	12510.39	12510.8	ADR-0110394	12525.39	12525.1
ADR-0108479	12510.39	12510.8	ADR-0110485	12759.39	12759.1
ADR-0108498	12276.11	12275.7	ADR-0109977	12672.59	12672.3
ADR-0110684	11258.3	11257.9	ADR-0110409	12731.49	12731.2
Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0108486	12665.39	12665.1	ADR-0110462	12557.4	12557.6
ADR-0108490	12458.21	12458.5	ADR-0110652	12751.4	12751.6
ADR-0110449	12631.41	12631.7	ADR-0110715	12680.4	12680.2
ADR-0109981	12500.38	12500.1	ADR-0108482	12446.11	12446.3
ADR-0110423	12763.52	12763.8	ADR-0110452	12710.49	12710.3
ADR-0110685	12678.43	12678.7	ADR-0110451	12631.41	12631.6
ADR-0110700	12664.33	12664.6	ADR-0110026	12619.49	12619.3
ADR-0110053	12580.43	12580.7	ADR-0110047	12515.38	12515.2
ADR-0110662	12834.43	12834.7	ADR-0108489	12506.42	12506.6
ADR-0110375	12554.36	12554.1	ADR-0110381	12498.37	12498.2
ADR-0110661	12826.44	12826.7	ADR-0110698	12664.33	12664.5
ADR-0110413	12703.46	12703.2	ADR-0110472	12568.43	12568.6
ADR-0110393	12554.36	12554.1	ADR-0110477	12586.43	12586.6
ADR-0110377	12552.35	12552.1	ADR-0110054	12580.43	12580.6
ADR-0110761	12747.45	12747.2	ADR-0110056	12580.43	12580.6
ADR-0110493	12917.55	12917.8	ADR-0108511	12333.13	12333.3
ADR-0110727	12638.35	12638.6	ADR-0110039	12580.43	12580.6
ADR-0110481	12755.44	12755.2	ADR-0110050	12580.43	12580.6

ADR-0110517	12611.34	12611.1	ADR-0110699	12664.33	12664.5
ADR-0108488	12348.26	12348.5	ADR-0110478	12570.36	12570.2
ADR-0110676	12826.44	12826.2	ADR-0110680	12676.36	12676.2
ADR-0110518	12611.34	12611.1	ADR-0110659	12826.44	12826.6
ADR-0110483	12767.47	12767.7	ADR-0110044	12594.46	12594.3
ADR-0110432	12648.33	12648.1	ADR-0110682	11955.86	11956
ADR-0110015	12536.37	12536.6	ADR-0110683	11596.56	11596.7
ADR-0108510	12317.13	12316.9	ADR-0110038	12594.46	12594.6
ADR-0110011	12536.37	12536.6	ADR-0110455	12643.44	12643.3
ADR-0110448	12643.37	12643.6	ADR-0110002	12524.34	12524.2
ADR-0110479	12584.42	12584.2	ADR-0110693	12664.33	12664.2
ADR-0110725	12650.38	12650.6	ADR-0110010	12536.37	12536.5
ADR-0110476	12614.42	12614.2	ADR-0110009	12536.37	12536.5
ADR-0110025	12619.49	12619.7	ADR-0110696	12664.33	12664.2
ADR-0110444	12647.41	12647.2	ADR-0110417	12699.42	12699.3
ADR-0110526	12777.49	12777.7	ADR-0110412	12715.42	12715.3
ADR-0108502	12276.11	12275.9	ADR-0110441	12663.48	12663.6
ADR-0110018	12619.49	12619.7	ADR-0110033	12619.49	12619.6
ADR-0110019	12619.49	12619.7	ADR-0110036	12619.49	12619.6
ADR-0110021	12619.49	12619.7	ADR-0110419	12715.49	12715.6
ADR-0110023	12619.49	12619.7	ADR-0110450	12548.29	12548.4
ADR-0110028	12619.49	12619.7	ADR-0110035	12619.49	12619.6
ADR-0110029	12619.49	12619.7	ADR-0108517	13038.71	13038.6
ADR-0110379	12541.4	12541.2	ADR-0110024	12619.49	12619.6
ADR-0110386	12498.3	12498.1	ADR-0110030	12619.49	12619.6
ADR-0110428	12842.6	12842.4	ADR-0110031	12619.49	12619.6
ADR-0110471	12554.4	12554.2	ADR-0110521	12615.29	12615.4
ADR-0110040	12568.4	12568.2	ADR-0110489	12913.6	12913.5
ADR-0109980	12742.6	12742.4	ADR-0110490	12913.6	12913.5
Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass
ADR-0110668	12751.4	12751.5	ADR-0110401	12542.35	12542.4
ADR-0110654	12751.4	12751.5	ADR-0110527	12773.45	12773.5
ADR-0110459	12557.4	12557.5	ADR-0110433	12731.45	12731.4
ADR-0110468	12572.41	12572.5	ADR-0110764	12747.45	12747.4
ADR-0110032	12619.49	12619.4	ADR-0110658	12826.44	12826.4
ADR-0110728	12664.41	12664.5	ADR-0109979	12642.56	12642.6
ADR-0110681	12319.13	12319.2	ADR-0110664	12676.36	12676.4
ADR-0110405	12735.53	12735.6	ADR-0110404	12735.53	12735.5
ADR-0110520	12619.33	12619.4	ADR-0110012	12536.37	12536.4
ADR-0110007	12536.37	12536.3	ADR-0108493	12312.17	12312.2
ADR-0110005	12536.37	12536.3	ADR-0110041	12580.43	12580.4
ADR-0110006	12536.37	12536.3	ADR-0110422	12763.52	12763.5
ADR-0108513	12333.13	12333.2	ADR-0110528	12785.48	12785.5
ADR-0110446	12742.56	12742.5	ADR-0110440	12663.48	12663.5
ADR-0108477	12316.14	12316.2	ADR-0110020	12619.49	12619.5
ADR-0110665	12676.36	12676.3	ADR-0110492	12921.59	12921.6
			ADR-0110436	12826.6	12826.6

Oligonucleotide	Molecular Weight	Observed Mass	Oligonucleotide	Molecular Weight	Observed Mass

ADR-0111146	12654.3	12653.3	ADR-0111148	12682.3	12684.4
ADR-0111148	12684.4	12683.3	ADR-0111149	12668	12668.3
ADR-0111774	12638.3	12638.1	ADR-0111150	12638	12638.3
ADR-0111776	12629.3	12628.2	ADR-0111151	12679.5	12680.3
ADR-0111802	12639.3	12638.5	ADR-0111152	12661.3	12662.3
ADR-0111818	12668.4	12669.6	ADR-0111153	12691.7	12692.3
ADR-0111820	12645.3	12645.6	ADR-0111154	12673.9	12674.4
ADR-0111846	12669.3	12669.2	ADR-0111155	12671.2	12672.3
ADR-0112336	12630.3	12629.6	ADR-0111156	12652.2	12654.3
ADR-0112337	12645.3	12643.5	ADR-0111157	12682.5	12684.4
ADR-0112338	12655.3	12654.1	ADR-0111158	12682.4	12684.4
ADR-0112339	12646.3	12646.1	ADR-0111159	12667.2	12668.3
ADR-0112340	12614.3	12613.7	ADR-0111160	12638	12638.3
ADR-0112341	12615.3	12614.4	ADR-0111161	12678.7	12680.3
ADR-0112342	12662.4	12662.5	ADR-0111162	12661.6	12662.3
ADR-0112343	12621.3	12620.1	ADR-0111163	12691.8	12692.3
ADR-0112344	12651.4	12651.6	ADR-0111164	12673.8	12674.4
ADR-0112345	12614.3	12613.8	ADR-0111165	12764.1	12765.4
ADR-0112346	12597.3	12597.4	ADR-0111166	12685.6	12686.3
ADR-0112347	12627.3	12626.2	ADR-0111167	12667.6	12668.4
ADR-0112348	12646.3	12646.7	ADR-0111168	12697.7	12698.4
ADR-0112349	12661.3	12660.6	ADR-0111169	12697.7	12698.4
ADR-0112350	12685.3	12685.4	ADR-0111170	12680.9	12682.3
ADR-0112351	12662.3	12662.2	ADR-0111171	12651.7	12652.4
ADR-0112352	12644.3	12643	ADR-0111172	12693.6	12694.3
ADR-0112353	12627.3	12626.6	ADR-0111173	12674.7	12676.3
ADR-0112354	12657.3	12657.6	ADR-0111174	12705	12706.4
ADR-0112355	12692.4	12692.2	ADR-0111175	12687	12688.4
ADR-0112356	12651.4	12651.5	ADR-0111179	12671.3	12672.3
ADR-0112357	12681.4	12680.9	ADR-0111180	12652.2	12654.3
ADR-0112358	12644.3	12643.1	ADR-0111181	12682.9	12684.4
ADR-0112359	12627.3	12626.5	ADR-0111182	12667.2	12668.3
ADR-0112360	12657.3	12658	ADR-0111183	12625.3	12626.3
ADR-0112361	12652.4	12651.9	ADR-0111184	12679.5	12680.3
ADR-0112362	12606.3	12605.4	ADR-0111185	12661.5	12662.3
ADR-0112363	12575.3	12574.8	ADR-0110657	12830.5	12829.6
ADR-0112364	12572.3	12572.1	ADR-0111146	12654.3	12653.9
ADR-0112365	12652.4	12651.8	ADR-0111148	12684.4	12685
ADR-0112366	12718.4	12718.2	ADR-0111774	12638.3	12638.3
ADR-0112367	12655.3	12654.5	ADR-0111775	12661.4	12662
ADR-0112368	12655.3	12654.3	ADR-0111776	12629.3	12629.4
ADR-0112369	12701.4	12702	ADR-0111777	12615.3	12614.3
ADR-0112370	12621.3	12619.9	ADR-0111778	12598.3	12598

ADR-0112371	12621.3	12620.9	ADR-0111779	12612.3	12612.5
ADR-0112372	12638.3	12638.6	ADR-0111780	12678.4	12679.3
ADR-0112373	12575.3	12574.5	ADR-0111781	12678.4	12679.2
ADR-0112374	12575.3	12574.4	ADR-0111782	12615.3	12615.4
ADR-0112375	12592.3	12591.8	ADR-0111783	12678.4	12679.3
ADR-0112376	12592.3	12591.8	ADR-0111784	12661.4	12662.1
ADR-0112377	12575.3	12574.5	ADR-0111785	12598.3	12598
ADR-0112378	12558.3	12559	ADR-0111786	12661.4	12662.4
ADR-0112379	12638.3	12638.2	ADR-0111787	12615.3	12614.5
ADR-0112381	12670.3	12669.5	ADR-0111788	12598.3	12598
ADR-0112382	12639.3	12638.9	ADR-0111789	12615.3	12615.3
ADR-0112384	12580.3	12579.9	ADR-0111790	12615.3	12615
ADR-0112385	12640.3	12639.5	ADR-0111791	12615.3	12615.1
ADR-0112387	12655.3	12653.6	ADR-0111792	12598.3	12597.9
ADR-0112388	12663.4	12662.9	ADR-0111793	12598.3	12598
ADR-0112389	12647.4	12646.7	ADR-0111794	12678.4	12679.4
ADR-0112391	12678.4	12678.7	ADR-0111795	12629.3	12630.2
ADR-0112392	12639.3	12638.7	ADR-0111796	12598.3	12598.1
ADR-0112393	12639.3	12639	ADR-0111797	12644.4	12643.4
ADR-0112394	12670.3	12669.8	ADR-0111798	12654.3	12653.7
ADR-0112395	12670.3	12670	ADR-0111799	12654.3	12653.5
ADR-0112396	12639.3	12639.3	ADR-0111800	12605.3	12604.9
ADR-0112398	12624.3	12624.1	ADR-0111801	12549.2	12549.4
ADR-0111862	12638.3	12638.5	ADR-0111802	12639.3	12639.2
ADR-0111863	12668.4	12668.8	ADR-0111803	12639.3	12639.5
ADR-0111148	12684.4	12685.3	ADR-0111804	12654.3	12654.1
ADR-0111864	12668.4	12669.4	ADR-0111805	12639.3	12639.2
ADR-0111865	12698.4	12698.1	ADR-0111806	12644.4	12644
ADR-0109982	12554.9	12556.4	ADR-0111807	12593.3	12593
ADR-0110420	12667.1	12668.4	ADR-0111808	12644.4	12644
ADR-0110652	12750.9	12751.4	ADR-0111809	12593.3	12593.4
ADR-0110667	12750.5	12751.4	ADR-0111810	12654.3	12653.4
ADR-0110922	12689.1	12690.5	ADR-0111811	12654.3	12653.8
ADR-0111098	12614.5	12615.3	ADR-0111812	12654.3	12653.5
ADR-0111099	12658.2	12659.4	ADR-0111813	12605.3	12604.9
ADR-0111100	12562.6	12564.2	ADR-0111814	12605.3	12604.9
ADR-0111101	12663	12664.2	ADR-0111815	12639.3	12639
ADR-0111102	12618.3	12619.3	ADR-0111816	12654.3	12653.9
ADR-0111103	12662.7	12663.4	ADR-0111817	12623.3	12622.6
ADR-0111104	12666.7	12668.3	ADR-0111818	12668.4	12669.6
ADR-0111105	12712.5	12714.5	ADR-0111819	12691.4	12692.2
ADR-0111106	12757.5	12758.5	ADR-0111820	12645.3	12646
ADR-0111107	12662.7	12663.4	ADR-0111821	12645.3	12645.6

ADR-0111108	12762.8	12763.4	ADR-0111822	12628.3	12628.3
ADR-0111109	12621.3	12623.4	ADR-0111823	12642.4	12643
ADR-0111110	12571.4	12572.3	ADR-0111824	12708.4	12708.9
ADR-0111111	12670.2	12672.3	ADR-0111825	12708.4	12708.8
ADR-0111112	12621.5	12623.3	ADR-0111826	12645.3	12646.1
ADR-0111113	12665.9	12667.3	ADR-0111827	12708.4	12708.7
ADR-0111114	12670.1	12672.2	ADR-0111828	12691.4	12692.2
ADR-0111115	12618.4	12619.3	ADR-0111829	12628.3	12629.2
ADR-0111116	12567	12568.2	ADR-0111830	12691.4	12692.5
ADR-0111117	12666.7	12668.3	ADR-0111831	12645.3	12645.7
ADR-0111118	12712.8	12714.5	ADR-0111832	12628.3	12628.4
ADR-0111119	12662.3	12663.4	ADR-0111833	12645.3	12645.6
ADR-0111120	12762.9	12763.4	ADR-0111834	12645.3	12646.1
ADR-0111121	12720.1	12722.5	ADR-0111835	12645.3	12645.6
ADR-0111122	12748.5	12750.5	ADR-0111836	12628.3	12628.5
ADR-0111123	12862.7	12864.6	ADR-0111837	12628.3	12628.5
ADR-0111124	12720.6	12722.5	ADR-0111838	12708.4	12708.6
ADR-0111125	12748.1	12750.5	ADR-0111839	12659.3	12659.4
ADR-0111126	12862.6	12864.6	ADR-0111840	12628.3	12629
ADR-0111127	12717.1	12718.5	ADR-0111841	12674.4	12675
ADR-0111128	12745.8	12746.5	ADR-0111842	12628.3	12628.2
ADR-0111129	12858.9	12860.6	ADR-0111843	12684.4	12685.5
ADR-0111130	12704.3	12706.5	ADR-0111844	12635.4	12634.7
ADR-0111131	12732.6	12734.5	ADR-0111845	12579.3	12580.8
ADR-0111132	12878.7	12880.7	ADR-0111846	12669.3	12669.7
ADR-0111133	12792	12793.5	ADR-0111847	12669.3	12669.8
ADR-0111134	12819.5	12821.5	ADR-0111848	12684.4	12685.5
ADR-0111135	12966.9	12967.7	ADR-0111849	12669.3	12669.4
ADR-0111136	12732.2	12733.4	ADR-0111850	12662.4	12663.4
ADR-0111137	12762.9	12763.4	ADR-0111851	12623.3	12625.3
ADR-0111138	12762.5	12763.4	ADR-0111852	12674.4	12674.6
ADR-0111139	12746.6	12747.4	ADR-0111853	12623.3	12624.7
ADR-0111140	12715.9	12717.4	ADR-0111854	12684.4	12685.5
ADR-0111141	12758.1	12759.4	ADR-0111855	12684.4	12685.2
ADR-0111142	12739.5	12741.4	ADR-0111856	12684.4	12685.6
ADR-0111143	12769.7	12771.4	ADR-0111857	12635.4	12637.2
ADR-0111144	12752.2	12753.4	ADR-0111858	12635.4	12637.4
ADR-0111145	12670.4	12672.3	ADR-0111859	12669.3	12669.4
ADR-0111146	12653.3	12654.3	ADR-0111860	12684.4	12685.4
ADR-0111147	12682.2	12684.4	ADR-0111861	12653.3	12653.4
ADR-0111146	12653.3	12654.3	ADR-0112361	12651.9	12652.4
ADR-0111148	12683.3	12684.4	ADR-0112362	12605.4	12606.3
ADR-0111774	12638.1	12638.3	ADR-0112363	12574.8	12575.3

ADR-0111776	12628.2	12629.3	ADR-0112364	12572.1	12572.3
ADR-0111802	12638.5	12639.3	ADR-0112365	12651.8	12652.4
ADR-0111818	12669.6	12668.4	ADR-0112366	12718.2	12718.4
ADR-0111820	12645.6	12645.3	ADR-0112367	12654.5	12655.3
ADR-0111846	12669.2	12669.3	ADR-0112368	12654.3	12655.3
ADR-0112336	12629.6	12630.3	ADR-0112369	12702	12701.4
ADR-0112337	12643.5	12645.3	ADR-0112370	12619.9	12621.3
ADR-0112338	12654.1	12655.3	ADR-0112371	12620.9	12621.3
ADR-0112339	12646.1	12646.3	ADR-0112372	12638.6	12638.3
ADR-0112340	12613.7	12614.3	ADR-0112373	12574.5	12575.3
ADR-0112341	12614.4	12615.3	ADR-0112374	12574.4	12575.3
ADR-0112342	12662.5	12662.4	ADR-0112375	12591.8	12592.3
ADR-0112343	12620.1	12621.3	ADR-0112376	12591.8	12592.3
ADR-0112344	12651.6	12651.4	ADR-0112377	12574.5	12575.3
ADR-0112345	12613.8	12614.3	ADR-0112378	12559	12558.3
ADR-0112346	12597.4	12597.3	ADR-0112379	12638.2	12638.3
ADR-0112347	12626.2	12627.3	ADR-0112381	12669.5	12670.3
ADR-0112348	12646.7	12646.3	ADR-0112382	12638.9	12639.3
ADR-0112349	12660.6	12661.3	ADR-0112384	12579.9	12580.3
ADR-0112350	12685.4	12685.3	ADR-0112385	12639.5	12640.3
ADR-0112351	12662.2	12662.3	ADR-0112387	12653.6	12655.3
ADR-0112352	12643	12644.3	ADR-0112388	12662.9	12663.4
ADR-0112353	12626.6	12627.3	ADR-0112389	12646.7	12647.4
ADR-0112354	12657.6	12657.3	ADR-0112391	12678.7	12678.4
ADR-0112355	12692.2	12692.4	ADR-0112392	12638.7	12639.3
ADR-0112356	12651.5	12651.4	ADR-0112393	12639	12639.3
ADR-0112357	12680.9	12681.4	ADR-0112394	12669.8	12670.3
ADR-0112358	12643.1	12644.3	ADR-0112395	12670	12670.3
ADR-0112359	12626.5	12627.3	ADR-0112396	12639.3	12639.3
ADR-0112360	12658	12657.3	ADR-0112398	12624.1	12624.3
ADR-0111146	12653.6	12654.3	ADR-0111148	12685.3	12684.4
ADR-0111862	12638.5	12638.3	ADR-0111864	12669.4	12668.4
ADR-0111863	12668.8	12668.4	ADR-0111865	12698.1	12698.4
ADR-0112416	13014.63	13016.1	ADR-0112411	13159.68	13159.5

Example 12. Provided technologies can provide editing.

[01185] Oligonucleotides comprising various types of sugars, nucleobases, internucleotidic linkages, and stereochemistry and patterns thereof were designed and assessed, including those comprising PO internucleotidic linkages, PS internucleotidic linkages, PN (e.g., phosphoryl guanidine linkages such as n001 and n025) internucleotidic linkages, various nucleobases (e.g., modified nucleobases, e.g., [3nU]), sugars (e.g., 2'-F, 2'-OMe, 2'-MOE, natural DNA sugar), controlled stereochemistry, patterns thereof, etc. as described herein. Certain data are presented in Figure 10, Figure 11, Figure 12, Figure 13, Figure 14, Figure 15, Figure

16, and Figure 17. Primary human hepatocytes homozygous for M148 mutation were dosed with indicated concentrations of indicated oligonucleotides via gymnotic uptake. Oligonucleotides targeted adenosine in M148 codon (i.e., AUG) of mutant PNPLA3 to produce A-to-I editing, resulting in the transcript being read as a valine codon (i.e., GUG). At 72 hours following oligonucleotide addition, cells were harvested and RNA collected. RNA was used to produce cDNA, which was subsequently used for Sanger sequencing to quantify RNA editing.

[01186] Relative EC50 and EC Max values corresponding to Figure 13 and Figure 14 are shown in the tables below.

Oligonucleotide	Relative EC50 (uM)	EC Max (uM)
ADR-0110652	0.02083	51.89
ADR-0111146	0.02119	63.02
ADR-0110667	0.02148	55.51
ADR-0111148	0.02149	56.4
ADR-0110481	0.02934	59.19
ADR-0110420	0.03542	70.31

[01187] Relative EC50 and EC Max values corresponding to the first portion of Figure 15 are shown in the table below.

Oligonucleotide	Relative EC50 (uM)	EC Max (uM)
ADR-0111776	0.01172	68.45591
ADR-0111820	0.01449	67.21593
ADR-0110652	0.01483	59.69151
ADR-0110667	0.01666	60.37811
ADR-0110481	0.01846	64.75257
ADR-0111146	0.01883	71.03857
ADR-0111148	0.01928	68.5224
ADR-0110420	0.02162	77.39253

[01188] Relative EC50 and EC Max values corresponding to the second portion of Figure 15 are shown in the table below.

Oligonucleotide	Relative EC50 (uM)	EC Max (uM)
ADR-0111820	0.01235	59.84429
ADR-0111776	0.0128	62.1387
ADR-0110652	0.01299	46.61544
ADR-0110481	0.01343	48.82329
ADR-0110667	0.01433	48.76712
ADR-0111146	0.01563	57.69511
ADR-0111148	0.01661	54.2735
ADR-0110420	0.02739	69.35705

[01189] In some embodiments, oligonucleotides comprising a 2`-OMe modification and [3nU] at a

nucleoside opposite to a target adenosine can provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a 2'-OMe modification and [3nU] at a nucleoside opposite to a target adenosine). In some embodiments, oligonucleotides comprising one or more PN internucleotidic linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without a one or more PN linkages (e.g., between position N_{11} and N_{12} and/or position N_{12} and N_{13})). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_9). In some embodiments, oligonucleotides comprising one or more mismatches and/or wobble base pairs (e.g., a mismatch at position N_{20}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more mismatches and/or wobble base pairs (e.g., a mismatch or wobble base pair at position N_{20}). In some embodiments, oligonucleotides comprising one or more m1d sugars (e.g., at position N_{24}, N_{16}, N_{15}, N_9, or N_7) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more m1d sugars). In some embodiments, oligonucleotides comprising one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more 2'-MOE modifications (e.g., one or more 2'-MOE modifications at the 5' end of an oligonucleotide)). In some embodiments, oligonucleotides comprising one or more 2'-OMe modifications (e.g., one or more 2'-OMe modifications at one or more of N_{11}, N_{12}, and N_{13}) may provide comparable or increased levels of editing activity as compared to a reference oligonucleotide (e.g., an oligonucleotide without one or more 2'-OMe modifications (e.g., one or more 2'-OMe modifications at one or more of N_{11}, N_{12}, and N_{13})). Among other things, the present disclosure demonstrates that certain designs, e.g., certain nucleobases (e.g., modified nucleobases, nucleobases leading to mismatches, etc.), sugars, linkages, etc. at certain positions and combinations thereof can provide higher editing levels than others.

[01190] While various embodiments have been described and illustrated herein, those of ordinary skill in the art will readily envision a variety of other means and/or structures for performing the functions and/or obtaining the results and/or one or more of the advantages described in the present disclosure, and each of such variations and/or modifications is deemed to be included. More generally, those skilled in the art will readily appreciate that all parameters, dimensions, materials, and configurations described herein are meant to be example and that the actual parameters, dimensions, materials, and/or configurations may depend upon the specific application or applications for which the teachings of the present disclosure is/are used. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the embodiments of the present disclosure. It is, therefore, to be understood that the foregoing embodiments

are presented by way of example only and that, within the scope of the appended claims and equivalents thereto, claimed technologies may be practiced otherwise than as specifically described and claimed. In addition, any combination of two or more features, systems, articles, materials, kits, and/or methods, if such features, systems, articles, materials, kits, and/or methods are not mutually inconsistent, is included within the scope of the present disclosure.

CLAIMS

1. An oligonucleotide, wherein the oligonucleotide is an oligonucleotide selected from:

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[Ga

lNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0; and

RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0,

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

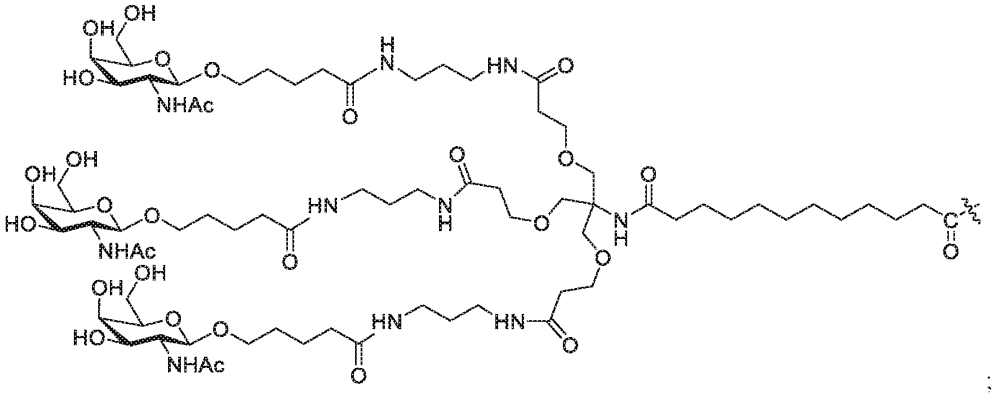
RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r]

](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0

or a salt thereof, wherein:

[GalNAc3C12oyl] represents



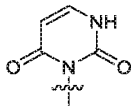
;

[nC6o] represents $-NH(CH_2)_6-$, wherein $-NH-$ is bonded to [GalNAc3C12oyl], and the end $-CH_2-$ is bonded to an oxygen atom that is bonded to the linkage phosphorus of a phosphate linkage;

d represents a natural DNA sugar in a nucleoside;

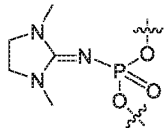
m represents a 2'-OMe modified sugar in a nucleoside;

[fl2r] represents a 2'-F modified sugar in a nucleoside;

[3nU] represents a nucleoside whose base is ;

p represents a phosphate linkage;

[Ssp] represents a phosphorothioate linkage in the *S*p configuration; and

[n001R] represents  wherein the phosphorus is of the *R*p configuration.

2. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

3. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[m

oe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

4. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

5. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

6. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

7. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

8. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

9. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{p.[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](

G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}|CHEM1{[nC6o]}|CHEM2{[GalNAc3C12oyl]}$CHEM1,RNA1,1:R1-1:R1|CHEM1,CHEM2,1:R2-1:R1$$$V2.0 or a salt thereof.

10. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

11. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

12. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].[fl2r](C)[n001R].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

13. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[n001R].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

14. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

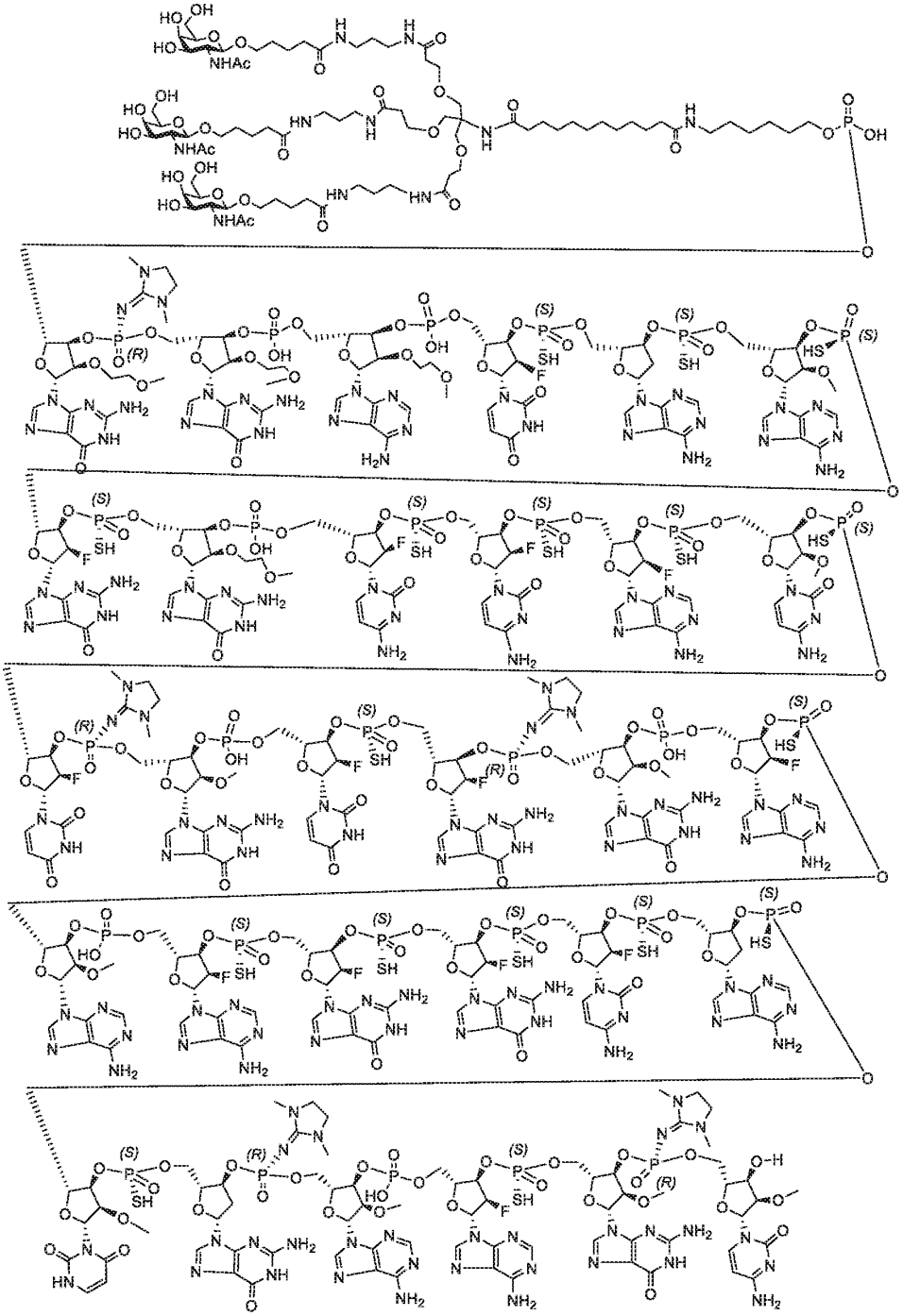
15. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(A)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](G)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

16. The oligonucleotide of claim 1, wherein the oligonucleotide is

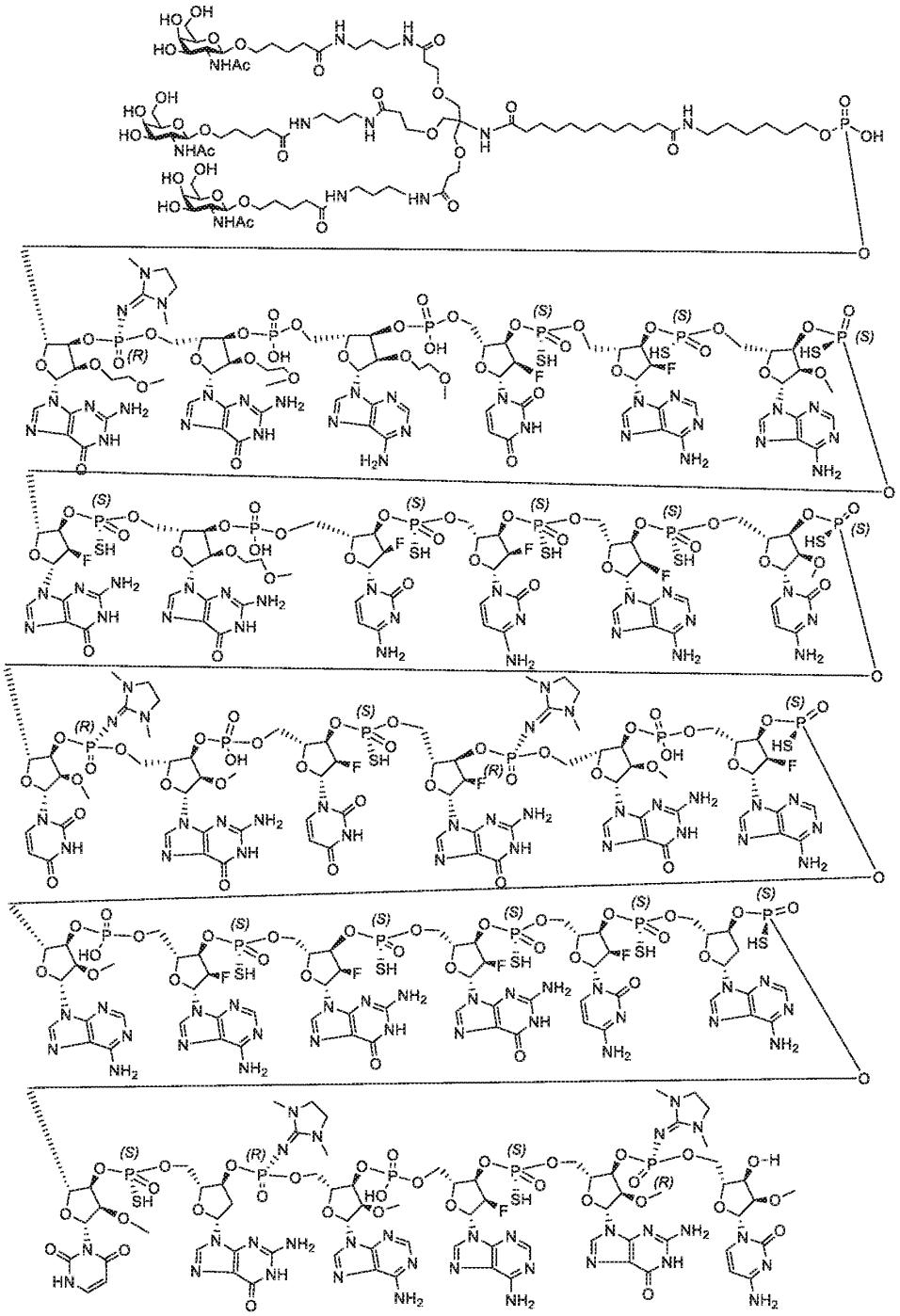
RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].[fl2r](U)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].m(U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

17. The oligonucleotide of claim 1, wherein the oligonucleotide is RNA1{[moe](G)[n001R].[moe](G)p.[moe](A)p.[fl2r](U)[Ssp].d(T)[Ssp].m(A)[Ssp].[fl2r](G)[Ssp].[moe](G)p.[fl2r](C)[Ssp].[fl2r](C)[Ssp].[fl2r](A)[Ssp].m(C)[Ssp].[fl2r](U)[n001R].m(G)p.[fl2r](U)[Ssp].[fl2r](A)[n001R].m(G)p.[fl2r](A)[Ssp].m(A)p.[fl2r](A)[Ssp].[fl2r](G)[Ssp].[fl2r](G)[Ssp].[fl2r](C)[Ssp].d(A)[Ssp].m([3nU])[Ssp].d(G)[n001R].m(A)p.[fl2r](A)[Ssp].m(G)[n001R].m(C)}$$$V2.0 or a salt thereof.

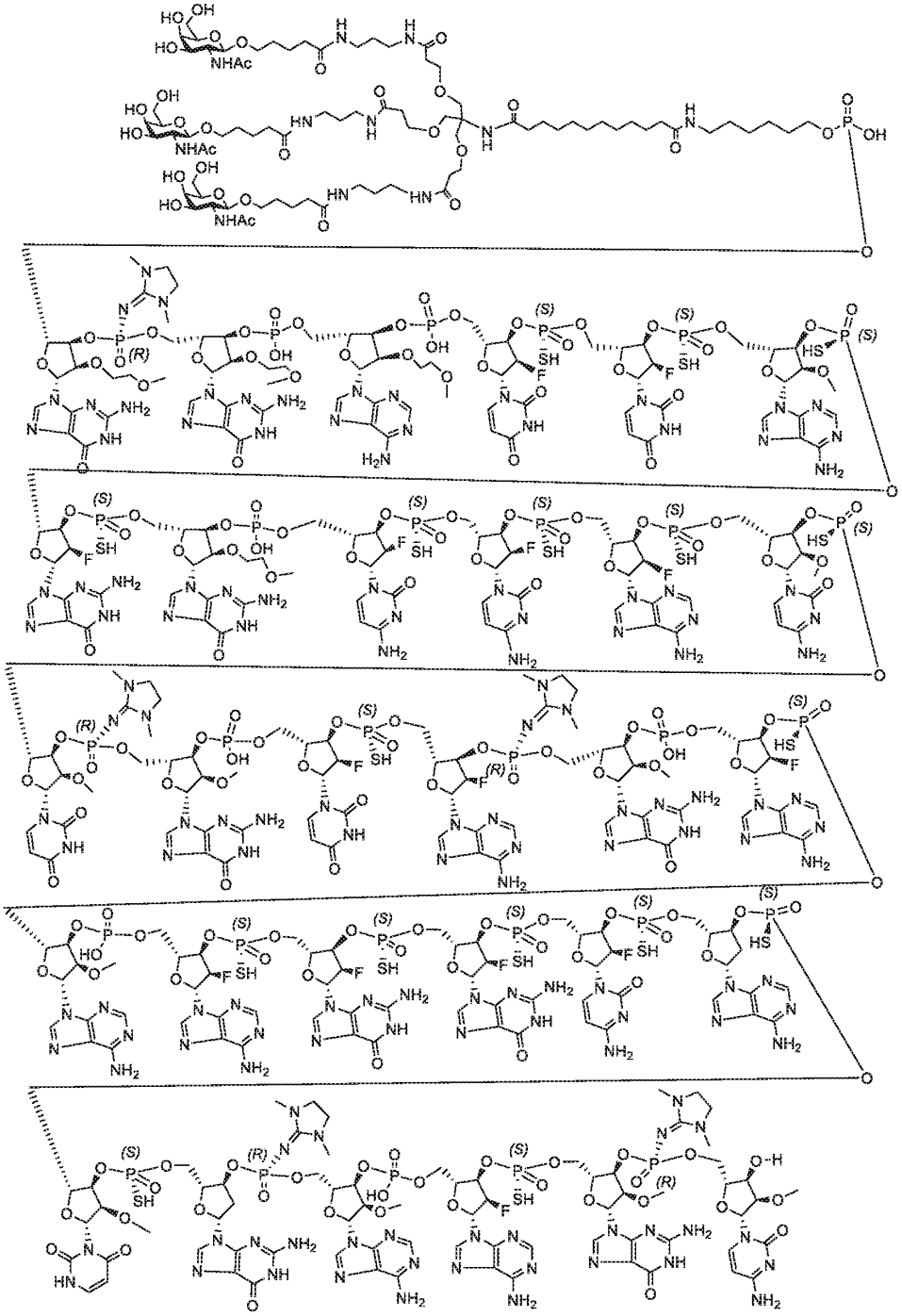
18. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



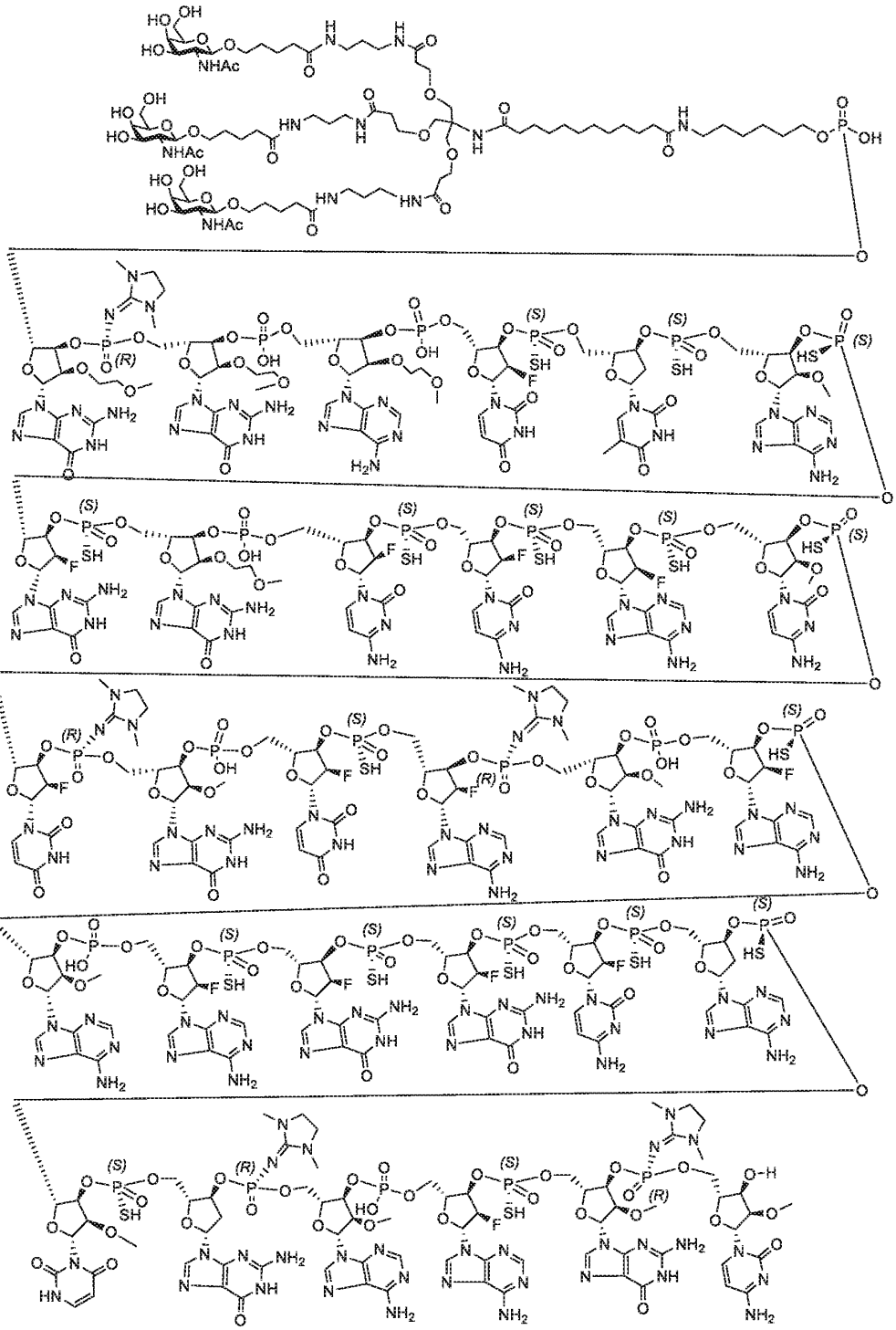
19. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



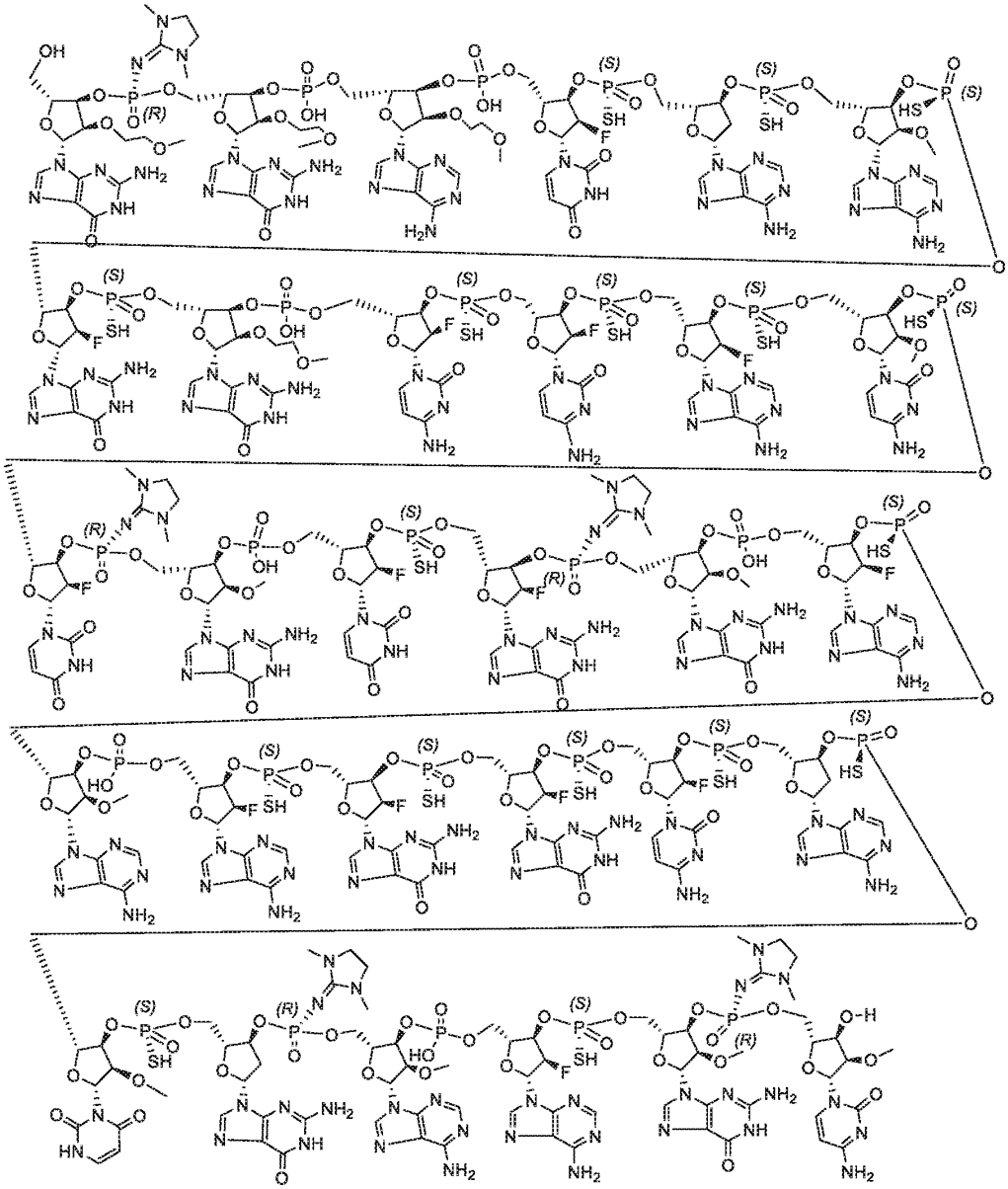
20. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



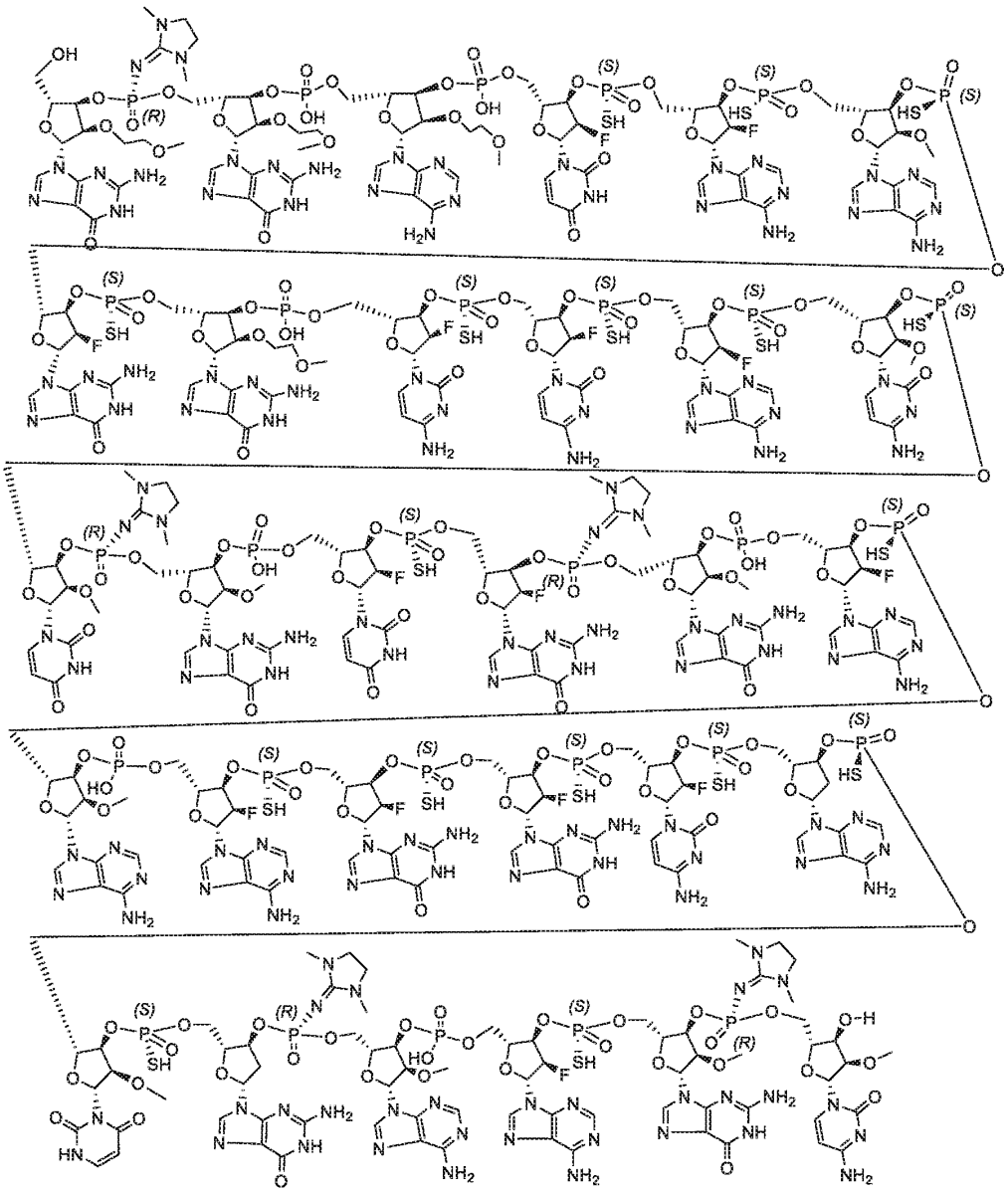
21. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



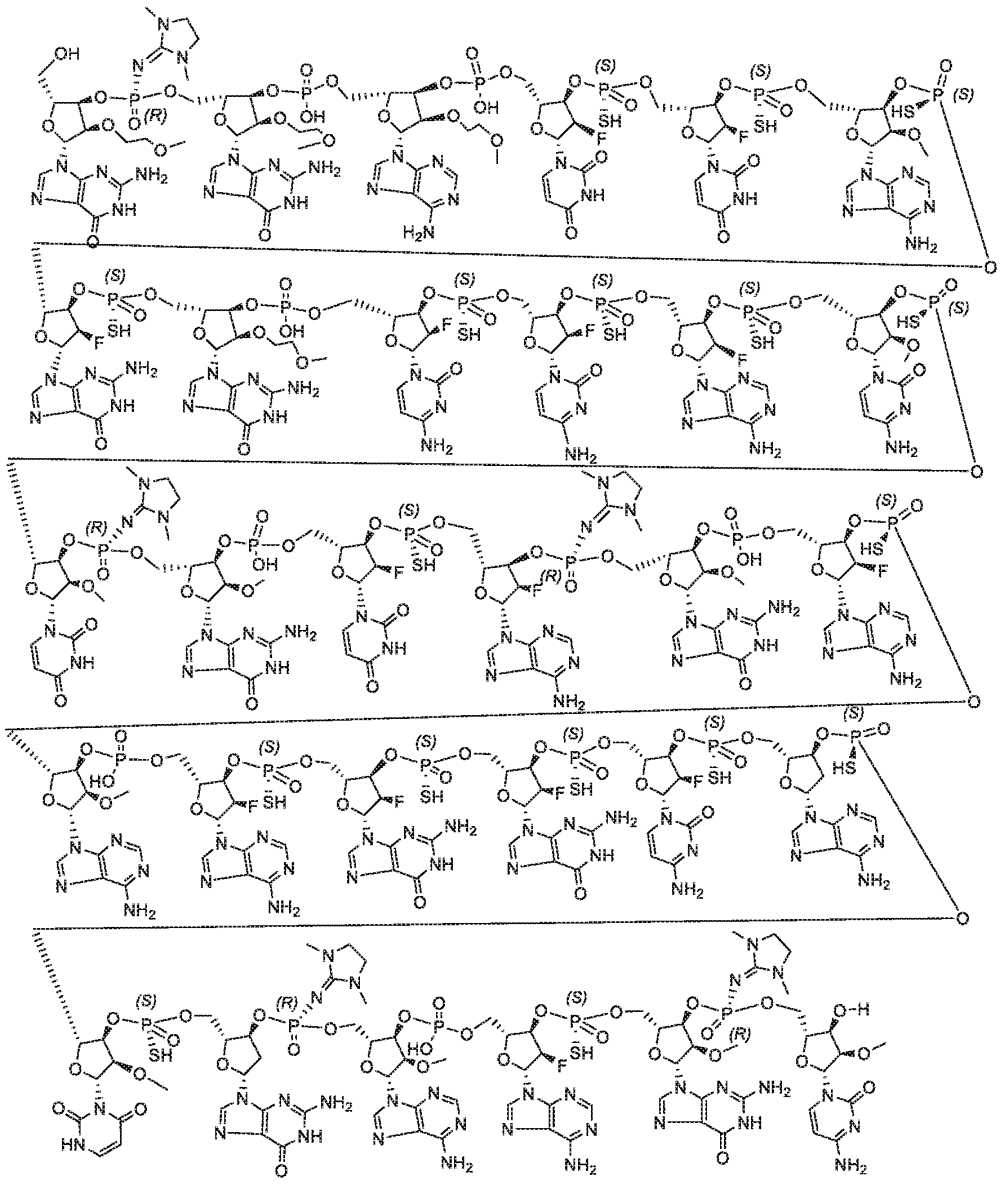
22. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



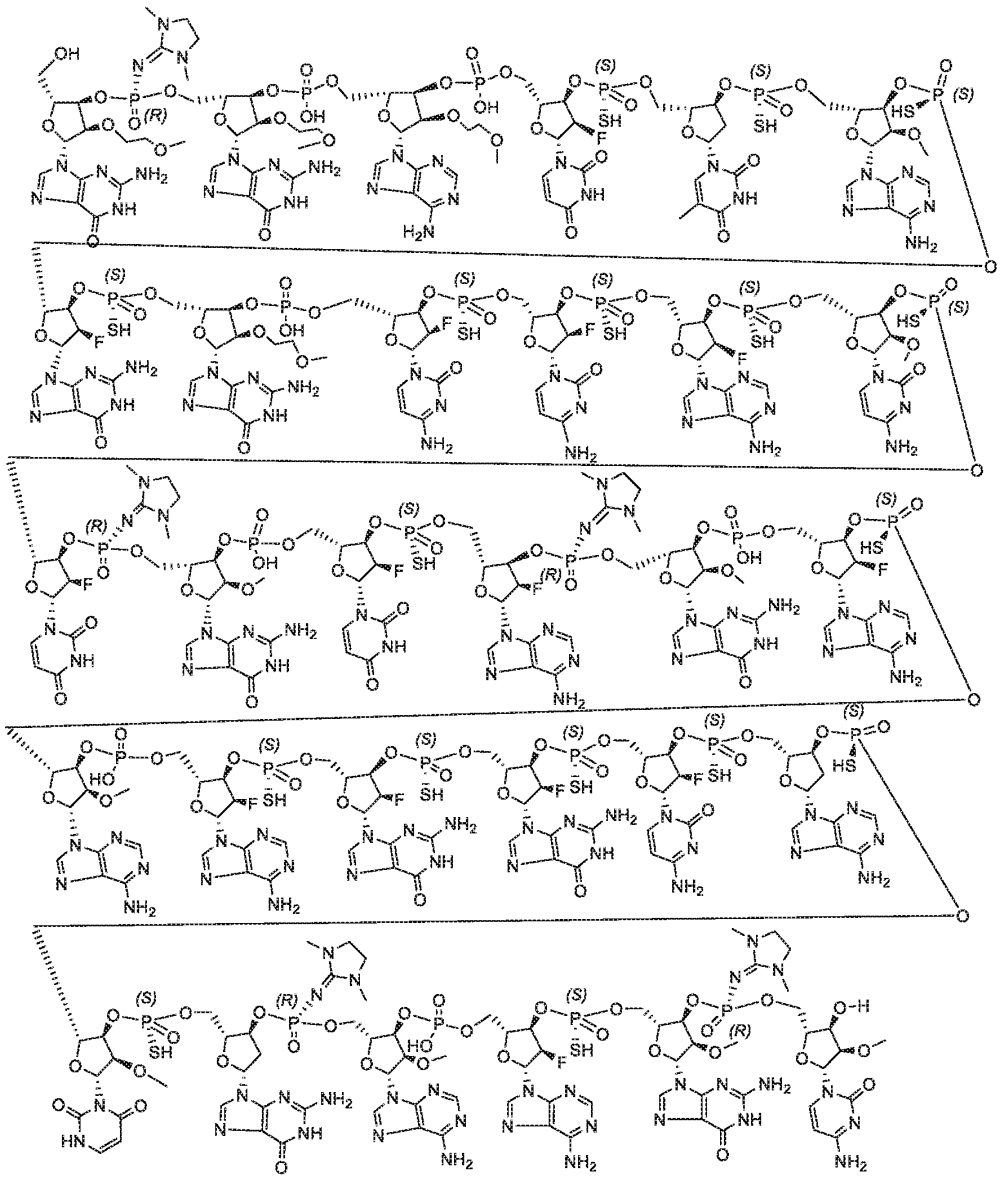
23. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



24. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



25. An oligonucleotide, wherein the oligonucleotide is the compound below or a salt thereof.



26. An oligonucleotide capable of hybridizing to a target sequence comprising GCUUCAUSCCUUUCUAC, wherein S is either G or C; or

an oligonucleotide capable of editing a target adenosine in a nucleic acid encoding a PNPLA3 polypeptide to produce a PNPLA3 polypeptide variant that differs by at least one amino acid residue; or

an oligonucleotide, wherein the base sequence of the oligonucleotide comprises at least 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 contiguous bases of a base sequence that is identical with or complementary to a base sequence of a PNPLA3 gene or a transcript thereof, wherein the oligonucleotide comprises one or more modified sugars, one or more modified nucleobases, and/or one or more modified internucleotidic

linkages; or

an oligonucleotide comprising 5'-$N_1N_0N_{-1}$-3', wherein N_1, N_0, and N_{-1} are each independently a nucleoside and are linked by internucleotidic linkages, wherein the oligonucleotide is capable of binding to a target nucleic acid with N_0 opposite to a target adenosine; or

an oligonucleotide comprising:

a first domain; and

a second domain,

wherein:

the first domain comprises one or more 2'-F modifications;

the second domain comprises one or more sugars that do not have a 2'-F modification; or

an oligonucleotide comprising a modified nucleobase, nucleoside, sugar or internucleotidic linkage as described in the present disclosure; or

an oligonucleotide, wherein about or at least about 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% of all sugars are 2'-F modified sugars; or

an oligonucleotide comprising a second subdomain as described in the present disclosure; or

an oligonucleotide comprising one or more modified sugars and/or one or more modified internucleotidic linkages, wherein the oligonucleotide comprises a first domain and a second domain each independently comprising one or more nucleobases.

27. The oligonucleotide of any one of the preceding claims, wherein:

1) the base sequence of the oligonucleotide comprises at least 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, or 30 contiguous bases of GGAUAAGGCCACUGUAGAAGGGGAUGAAGC, GGGACACGGUGAUGGAGAAGGGCAUGAAGC, AUAAGGCCACUGUAGAAGGGGAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGGAUGAAGC, AGGGAUAAGGCCACUAGAAGGGGAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGGAUGAAGC, GGAUAAGGCCACUGUAGAAGGGCAUGAAGC, GAUAAGGCCACUGUAGAAGGGCAUGAAGCA, AUAAGGCCACUGUAGAAGGGCAUGAAGCAG, GGGAUAAGGCCACUGAGAAGGGCAUGAAGC, AGGGAUAAGGCCACUAGAAGGGCAUGAAGC, AGGAGGGAUAAGGCCAGAAGGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCAUGAAGC, GAUAAGGCCACUGUAGAAAGGCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, GAUAACGCCACUGUAGAAAGCCAUGAAGCA, GAUAACGCCTCUGUAGAAAGCCAUGAAGCA, AUAAGGCCACUGUAGAAAGGCAUGAAGCAG, UAAGGCCACUGUAGAAAGGCAUGAAGCAGG, AAGGCCACUGUAGAAAGGCAUGAAGCAGGA, GGAUAAGGCCACUGUAGAAAGCCAUGAAGC, GGAUAAGGCCACUGUAGAAACGCAUGAAGC, GGAUAAGGCCACUGUAGAAUGGCAUGAAGC, GGAUAAGGCCACUGUAGAUAGGCAUGAAGC, GGAUAAGGCCACUGUAGUAAGGCAUGAAGC, GGAUAAGGCCACUGUACAAAGGCAUGAAGC, GGAUAAGGCCACUGUUGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGCGUGAAGC, GGAUAAGGCCACUGUAGAGAGGCAUGAAGC,

GGAUAAGGCCACUGUAGGAAGGCAUGAAGC, GGAUAAGGCCACUGUGGAAAGGCAUGAAGC, GGAUAAGGCCACUGUAGGGAGGCAUGAAGC, GGAUAAGGCCACUGUGGGGAGGCAUGAAGC, GGAUAAGGCCACUGUAGAAAGGUAUGAAGC, GGAUAAGGCCACUGUAGAAGGGUAUGAAGC, GGAUAAGGCCACUGUGGAAAGGUAUGAAGC,
GGGAUAAGGCCACUGUAGAAAGGCAUGAAGCA, or
GGAUAAGGCCACUGUAGAAAGGCAUGAAGCAG, wherein each T can be independently replaced with U and vice versa.

2) when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, a target adenosine in the target PNPLA3 transcript is modified;

3) when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of the target PNPLA3 transcript is reduced compared to absence of the product or presence of a reference oligonucleotide;

4) when the oligonucleotide is contacted with a target PNPLA3 transcript comprising a target adenosine in a system, level of a product of the target PNPLA3 transcript is altered compared to absence of the product or presence of a reference oligonucleotide;

5) level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is modified;

6) level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the target adenosine is replaced with inosine; and/or

7) level of a product is increased, wherein the product is or is encoded by a PNPLA3 transcript which is otherwise identical to the target PNPLA3 transcript but the adenine of the target adenosine is replaced with guanine.

28. The oligonucleotide of any one of claims 26-27, wherein the target adenosine is more associated with a condition, disorder or disease than a guanine at the same position.

29. The oligonucleotide of any one of the preceding claims from claim 26, wherein the oligonucleotide has a length of about 10-200 (e.g., about 10-20, 10-30, 10-40, 10-50, 10-60, 10-70, 10-80, 10-90, 10-100, 10-120, 10-150, 20-30, 20-40, 20-50, 20-60, 20-70, 20-80, 20-90, 20-100, 20-120, 20-150, 20-200, 25-30, 25-40, 25-50, 25-60, 25-70, 25-80, 25-90, 25-100, 25-120, 25-150, 25-200, 30-40, 30-50, 30-60, 30-70, 30-80, 30-90, 30-100, 30-120, 30-150, 30-200, 10, 20, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 50, 60, etc.) nucleobases, preferably wherein the oligonucleotide has a length of about 26-35 nucleobases.

30. The oligonucleotide of any one of the preceding claims from claim 26, wherein the oligonucleotide can hybridize to a PNPLA3 transcript, wherein the portion the oligonucleotide hybridizes to is, comprises, or overlaps with gcuucaucccccuucuacaguggccuuaucc or gcuucaugccuuucuacaguggccuuaucc.

31. The oligonucleotide of any one of the preceding claims from claim 26, wherein the first 3, 4, 5, 6, 7, 8, 9, 10 or more sugars from the 5'-end of the oligonucleotide independently comprise a 2'-OR modification,

wherein R is optionally substituted C_{1-6} aliphatic.

32. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{23} and N_{22} is a natural phosphate linkage, and/or wherein the 2nd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

33. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{22} and N_{21} is a natural phosphate linkage, and/or wherein the 3rd internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

34. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{17} and N_{16} is a natural phosphate linkage, and/or wherein the 8th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

35. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{11} and N_{10} is a natural phosphate linkage, and/or wherein the 14th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

36. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage or a PS internucleotidic linkage, and/or wherein the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage or a PS internucleotidic linkage.

37. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_8 and N_7 is a natural phosphate linkage, and/or wherein the 17th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

38. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_6 and N_5 is a natural phosphate linkage or a PS internucleotidic linkage, and/or wherein the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage or a PS internucleotidic linkage.

39. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_6 and N_5 is a natural phosphate linkage, and/or wherein the 19th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

40. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{-2} and N_{-3} is a natural phosphate linkage, and/or wherein the 27th internucleotidic linkage from the 5'-end of the oligonucleotide is a natural phosphate linkage.

41. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{24} and N_{23} is a PN linkage, and/or wherein the 1st internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

42. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{13} and N_{12} is a PN or a PS linkage, and/or wherein the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or PS linkage.

43. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{13} and N_{12} is a PS linkage, and/or wherein the 12th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage.

44. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{12} and N_{11} is a PN linkage, and/or wherein the 13th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

45. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_9 and N_8 is a PN or a PS linkage, and/or wherein the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or PS linkage.

46. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_9 and N_8 is a PN linkage, and/or wherein the 16th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

47. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a PN or a methylphosphonate linkage, and/or wherein the 26th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN or a methylphosphonate linkage.

48. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{-1} and N_{-2} is a PN linkage, and/or wherein the 26th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage.

49. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{-4} and N_{-5} is a PN linkage, and/or wherein the 29th internucleotidic linkage from the 5'-end of the oligonucleotide is a PN linkage, and/or wherein the first internucleotidic linkage from the 3'-end of the oligonucleotide is a PN internucleotidic linkage.

50. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_1 and N_0 is a PS linkage, and/or wherein the 24th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage.

51. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_0 and N_{-1} is a PS linkage, and/or wherein the 25th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage.

52. The oligonucleotide of any one of the preceding claims from claim 26, wherein the internucleotidic linkage between N_{-3} and N_{-4} is a PS linkage, and/or wherein the 28th internucleotidic linkage from the 5'-end of the oligonucleotide is a PS linkage.

53. The oligonucleotide of any one of the preceding claims from claim 26, wherein the first internucleotidic linkage of the 5'-end of oligonucleotide is a PN internucleotidic linkage.

54. The oligonucleotide of any one of the preceding claims from claim 26, wherein the first internucleotidic linkage of the 3'-end of oligonucleotide is a PN internucleotidic linkage.

55. The oligonucleotide of any one of the preceding claims from claim 26, wherein the PN

internucleotidic linkage is a phosphoramidate internucleotidic linkage.

56. The oligonucleotide of any one of the preceding claims from claim 26, wherein the PN internucleotidic linkage is a phosphoryl guanidine internucleotidic linkage.

57. The oligonucleotide of any one of claims 26-54, wherein the PN internucleotidic linkage is n001.

58. The oligonucleotide of any one of claims 26-54, wherein the PN internucleotidic linkage is n006.

59. The oligonucleotide of any one of claims 26-54, wherein the PN internucleotidic linkage is MsPA.

60. The oligonucleotide of any one of the preceding claims from claim 26, wherein the linkage phosphorus of the PN internucleotidic linkage is *R*p.

61. The oligonucleotide of any one of the preceding claims from claim 26, wherein each internucleotidic linkage is independently a natural phosphate linkage, a PS internucleotidic linkage, or a PN internucleotidic linkage.

62. The oligonucleotide of any one of the preceding claims from claim 26, wherein each PS internucleotidic linkage is independently a phosphorothioate internucleotidic linkage.

63. The oligonucleotide of any one of the preceding claims from claim 26, wherein each phosphorothioate internucleotidic linkage is independently *S*p.

64. The oligonucleotide of any one of the preceding claims from claim 26, wherein each PN internucleotidic linkage is independently a phosphoramidate internucleotidic linkage.

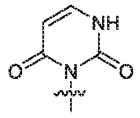
65. The oligonucleotide of any one of the preceding claims from claim 26, wherein the nucleobase of N_9 or the nucleobase of the 16th nucleoside from the 5'-end of the oligonucleotide is G or A.

66. The oligonucleotide of any one of claims 26-65, wherein the nucleobase of N_{20} or the 5th nucleoside from the 5'-end of the oligonucleotide is T, U or A.

67. The oligonucleotide of any one of the preceding claims from claim 26, wherein N_{24} is the first nucleoside.

68. The oligonucleotide of any one of claims 0-30, wherein the oligonucleotide consists of a first domain and a second domain, wherein the first domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases, and the second domain has a length of about 2-50 (e.g., about 5, 6, 7, 8, 9, or 10 - about 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, or about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40 or 50, etc.) nucleobases.

69. The oligonucleotide of any one of the preceding claims, wherein the nucleobase of N_0 is



70. The oligonucleotide of any one of the preceding claims from claim 26, wherein the sugar of N_0 is a

2'-OMe modified sugar.

71. The oligonucleotide of any one of the preceding claims from claim 26, wherein the sugar of N_1 is a natural DNA sugar, or a 2'-modified sugar.

72. The oligonucleotide of any one of the preceding claims, wherein the sugar of N_{-1} is a natural DNA sugar.

73. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of N_{-2} is a 2'-OMe modified sugar.

74. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of N_{-3} is a 2'-F modified sugar.

75. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of each of N_{24}, N_{23}, and/or N_{22} is independently a 2'-OR modified sugar, and/or wherein each of the 1st, 2nd and/or 3rd sugars from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar.

76. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of N_{27} is a 2'-OR modified sugar, and/or wherein the 8th sugar from the 5'-end of the oligonucleotide is a 2'-OR modified sugar.

77. The oligonucleotide of any one of claims 75-76, wherein the 2'-OR modified sugar is a 2'-MOE modified sugar.

78. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of each of N_{29}, N_{11}, and/or N_8 is independently a 2'-OR modified sugar, and/or wherein each of the 6th, 14th and 17th sugars from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar.

79. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of each of N_{-4}, and/or N_{-5} is independently a 2'-OR modified sugar, and/or wherein each of the last sugar and the second last sugar from the 5'-end of the oligonucleotide is independently a 2'-OR modified sugar.

80. The oligonucleotide of any one of claims 78-79, wherein the 2'-OR modified sugar is a 2'-OMe modified sugar.

81. The oligonucleotide of any one of the preceding claims from claim 26, wherein sugar of each of N_{21}, N_{18}, N_{16}, N_{15}, N_{14}, N_{10}, N_9, N_7, N_5, N_4, N_3 and/or N_2 is independently a 2'-F modified sugar, and/or wherein each of the 4th, 7th, 9th, 10th, 11th, 15th, 16th, 18th, 20th, 21st, 22nd and/or 23rd sugars from the 5'-end of the oligonucleotide is independently a 2'-F modified sugar.

82. The oligonucleotide of any one of the preceding claims from claim 26, wherein the oligonucleotide comprises an asialoglycoprotein receptor ligand.

83. An oligonucleotide comprising a duplexing region and a targeting region, wherein a targeting region is or comprises a second region of any one of the preceding claims, or 5'-$N_1N_0N_{-1}$-3' of any one of the preceding claims.

84. An oligonucleotide, which is a diastereomer of an oligonucleotide of any one of the preceding claims.

85. The oligonucleotide of any one of the preceding claims, wherein the oligonucleotide is in a salt form.

86. The oligonucleotide of any one of the preceding claims, wherein each chiral linkage phosphorus independently has a diastereomeric purity of about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, and/or wherein the diastereopurity of the oligonucleotide is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus.

87. The oligonucleotide of any one of the preceding claims, wherein the target adenosine is at a position within the PNPLA3 transcript encoding for I148M of a PNPLA3 polypeptide, and N_0 is opposite to the target adenosine.

88. A pharmaceutical composition comprising an oligonucleotide of any one of the preceding claims and a pharmaceutically acceptable carrier.

89. A chirally controlled composition comprising an oligonucleotide of any one of the preceding claims.

90. The composition of any one of claims 88-89, wherein each chiral linkage phosphorus of the oligonucleotide independently has a diastereomeric purity of about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, or wherein the diastereomeric purity of the oligonucleotide in the composition is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about or at least about 85%, 90%, 91%. 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%), and nc is the number of chiral linkage phosphorus in the oligonucleotide.

91. A composition comprising a plurality of oligonucleotides, wherein each oligonucleotides of the plurality is independently a particular oligonucleotide or a salt thereof, wherein the particular oligonucleotide is an oligonucleotide of any one of the preceding claims; or

an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally controlled internucleotidic linkages");

wherein each oligonucleotide of the plurality is independently an oligonucleotide of any one of the preceding claims (e.g., in an acid, base, or salt form); or

an oligonucleotide composition comprising a plurality of oligonucleotides, wherein oligonucleotides of the plurality share:

1) a common base sequence, and

2) the same linkage phosphorus stereochemistry independently at one or more (e.g., about 1-50, 1-40, 1-30, 1-25, 1-20, 1-15, 1-10, 5-50, 5-40, 5-30, 5-25, 5-20, 5-15, 5-10, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 or more) chiral internucleotidic linkages ("chirally

controlled internucleotidic linkages");

wherein the common base sequence is complementary to a base sequence of a portion of PNPLA3 transcript which portion comprises a target adenosine.

92. The composition of claim 91, wherein the level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about $(DS)^{nc}$, wherein DS is about 85%-100% (e.g., about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 99.5% or more) and nc is the number of chiral linkage phosphorus, or wherein the level of oligonucleotides of a plurality in oligonucleotides in the composition that share the common constitution of the plurality is about or at least about 20%-100%, or is about or at least about 20%-95%, 30%-90%, 40%-85%, 40%-80%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, or 90%.

93. A method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding claims; or

a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof in a subject, comprising converting the amino acid at position 148 of the PNPLA3 polypeptide into a valine; or

a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide; or

a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide; or

a method for producing a RNA encoding a PNPLA3 polypeptide that comprises I148V in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding claims; or

a method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in PNPLA3 in the genome of the subject, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide; or

a method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising editing a target adenosine in a transcript encoding the PNPLA3 polypeptide, wherein the target adenosine is in the codon encoding an amino acid at position 148 in the PNPLA3 polypeptide; or

a method for producing a PNPLA3 polypeptide comprising I148V in a subject, comprising administering or delivering to the subject an effective amount of an oligonucleotide or composition of any one of the preceding claims.

94. A method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in PNPLA3 in the genome of a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide; or

a method for preventing or treating a condition, disorder or disease, comprising editing a target adenosine in a PNPLA3 transcript in a subject susceptible thereto or suffering therefrom, wherein the target adenosine is in the codon encoding an amino acid at position 148 of a PNPLA3 polypeptide.

95. A method for preventing or treating a condition, disorder or disease, comprising administering or delivering to a subject susceptible thereto or suffering therefrom an effective amount of an oligonucleotide or composition of any one of the preceding claims.

96. The method of any one of claims 94-95, wherein the subject comprises an I148M mutation in PNPLA3, optionally wherein the subject is homozygous for the mutation.

97. The method of any one of claims 94-96, wherein:

the condition, disorder or disease is amenable to an A to G or A to I modification;

the condition, disease or disorder is associated with a PNPLA3 I148M mutation; and/or

the condition, disease or disorder is amenable to or can benefit from changing I148M to I148V in PNPLA3; and/or wherein:

the condition, disorder or disease is a liver condition, disorder or disease;

the condition, disorder or disease is a metabolic liver condition, disorder or disease;

the condition, disorder or disease is hepatitis;

the condition, disorder or disease is fibrosis;

the condition, disorder or disease is cirrhosis;

the condition, disorder or disease is hepatocellular

the condition, disorder or disease is steatosis;

the condition, disorder or disease is liver failure;

the condition, disorder or disease is metabolic dysfunction-associated steatohepatitis (MASH);

the condition, disorder or disease is nonalcoholic steatohepatitis (NASH); or

the condition, disorder or disease is non-alcoholic fatty liver disease (NAFLD).

98. The method of any one of the preceding claims, comprising assessment of liver fat and/or liver stiffness, and/or comprising liver biopsy, and/or comprising liver biopsy histology.

99. A method for modulating a protein interaction with an agent in a system wherein a protein is translated from its encoding RNA, comprising administering to the system an oligonucleotide or composition of any one of the preceding claims, wherein an adenosine in the encoding RNA is edited, wherein a protein is translated from the edited mRNA ("the edited protein"), wherein the edited protein differs from the unedited protein at an amino acid residue involving in the protein-agent interaction.

100. A method for delivering to a system an oligonucleotide, comprising administering to the system a conjugate of the oligonucleotide with an additional chemical moiety or a salt thereof.

101. A nucleic acid comprising a sequence of GCUUCIUSCCUUUCUAC, wherein:

S is either G or C; and

each U can be optionally and independently replaced with T; or

a nucleic acid comprising a sequence with about or at least about 50% sequence identity to GCUUCGUGCCUUUCUACAGUGGCCUUAUCC or GCUUCGUCCCCUUCUACAGUGGCCUUAUCC, wherein each U can be optionally and independently replaced with T; or

a polypeptide comprising an amino acid sequence with about or at least about 50% sequence identity to VDALVCSCFVPF or VDALVCSCFVPF, or a polypeptide comprising SEQ ID NO: 2 or a characteristic portion thereof; or

a cell comprising a nucleic acid above, and/or comprising or expressing the polypeptide above; or

a method for increasing lipase activity of a PNPLA3 polypeptide or characteristic portion thereof, comprising modifying an amino acid residue at a position that is or corresponds to position 148 of SEQ ID NO:2.

102. A method for preparing an oligonucleotide or composition of any one of the preceding claims, comprising utilizing a phosphoramidite (e.g., a phosphoramidite comprising a chiral auxiliary).

103. Use of an oligonucleotide or composition of any one of the preceding claims for editing a target adenosine in a codon, for preventing or treating a condition, disease or disorder, for manufacturing a medicament for preventing or treating a condition, disease or disorder, for a method of any one of the preceding claims, or for manufacturing a medicament for a method of any one of the preceding claims.

104. An oligonucleotide or composition of any one of the preceding claims, for preventing or treating a condition, disease or disorder, for manufacturing a medicament for preventing or treating a condition, disease or disorder, for use in a method of any one of the preceding claims, or for use in manufacturing a medicament for a method of any one of the preceding claims.

105. A nucleic acid, polypeptide, oligonucleotide, composition, use or method of any one of Embodiments 1-958.