

COMPOUNDS AND METHODS FOR MODULATING ALPHA-SYNUCLEIN EXPRESSION**Sequence Listing**

The present application is being filed along with a Sequence Listing in electronic format. The Sequence Listing is provided as a file entitled BIOL0468SEQ.xml, created on February 2, 2024, which is 3,338 KB in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field

Provided are compounds, pharmaceutical compositions, and methods for reducing the amount or activity of alpha-synuclein (SNCA) RNA in a cell or subject, and in certain instances reducing the amount of alpha-synuclein protein in a cell or subject. Such compounds, pharmaceutical compositions, and methods are useful to ameliorate at least one symptom or hallmark of a synucleinopathy (or alpha-synucleinopathy). Such symptoms and hallmarks include motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, and seizures. Such synucleinopathies include Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, and Alzheimer's disease.

Background

Alpha-synuclein is a small, highly charged 140-amino acid residue protein, predominantly expressed in central nervous system (CNS) neurons, where it is localized at presynaptic terminals in close proximity to synaptic vesicles (Iwai, et al., *Neuron*. 1995. 14: 467-475). Alpha-synuclein is encoded by the SNCA gene. Alpha-synuclein can associate with lipid membranes by forming amphipathic α -helices, as shown in vitro (Davidson, et al., *J. Biol. Chem.* 1998. 273: 9443-9449). Several studies suggest that alpha-synuclein is involved in modulating synaptic transmission, the density of synaptic vesicles, and neuronal plasticity (Cabin et al., *J. Neurosci.* 2002. 22: 8797-8807; Burre et al., *Science*. 2010. 329: 1663-1667; and Burre et al., *J. Neurosci.* 2015. 35: 5221-5232). It has been shown that SNCA inhibits synaptic vesicle release and disrupts the SNARE complex-mediated lipid membrane fusion (DeWitt et al., *Biochemistry*. 2013. 52: 2385-2387; Abeliovich et al., *Neuron*. 2000. 25: 239-252). Decreased SNARE-complex assembly is associated with neurological impairment, thus, indicating a link between presynaptic alpha-synuclein aggregates and neurodegeneration (Kramer and Schulz-Schaeffer, *J. Neurosci.* 2007. 27: 1405-1410). Knockout mouse models of alpha-synuclein are not lethal, and brain morphology is intact, suggesting that alpha-synuclein is not required for neuronal development and/or that compensatory pathways are present (Abeliovich et al., *Neuron*. 2000. 25: 239-252).

Misfolding, aggregation, and fibrillation of alpha-synuclein are implicated as critical factors in several neurodegenerative diseases, including, Parkinson's disease, Lewy body variant of Alzheimer's disease, diffuse Lewy body disease, dementia with Lewy bodies, and multiple system atrophy (Schulz-Schaeffer, *Acta Neuropathol.* 2010. 120: 131-143; Yoshida. *Neuropathology*. 2007. 27: 484-493). In each of these cases, alpha-synuclein protein is misfolded and assembles in aggregates in Lewy bodies and Lewy neurites (Uversky, *J. Neurochem.* 2007. 103: 17-37).

Point mutations, genomic duplications, or genomic triplications in SNCA have been associated with Parkinson's disease and other synucleinopathies. For example, six missense mutations in the SNCA gene have been

associated with autosomal dominant Parkinson's disease (A53T, A30P, E46K, H50Q, G51D, and A53E). The mutations are clustered within the membrane-binding domain, suggesting a contribution of this region to SNCA dysfunction. *See, e.g., Brás et al., Cells. 2021. 10: 375.*

Currently there is a lack of acceptable options for treating synucleinopathies such as Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, and Alzheimer's disease. It is therefore an objective herein to provide compounds, pharmaceutical compositions, and methods of use for the treatment of such synucleinopathies.

10 Summary

Provided herein are compounds, pharmaceutical compositions, and methods of use for reducing the amount or activity of SNCA RNA, and in certain embodiments reducing the amount of alpha-synuclein protein in a cell or subject. In certain embodiments, the subject has a synucleinopathy. In certain embodiments, the subject has Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain
15 embodiments, compounds useful for reducing the amount or activity of SNCA RNA are oligomeric compounds. In certain embodiments, compounds useful for reducing the amount or activity of SNCA RNA are modified oligonucleotides. In certain embodiments, compounds useful for reducing the amount of alpha-synuclein protein are oligomeric compounds. In certain embodiments, compounds useful for reducing the amount of alpha-synuclein protein
20 are modified oligonucleotides.

Also provided are methods useful for ameliorating at least one symptom or hallmark of a synucleinopathy. In certain embodiments, the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain embodiments, the symptom or hallmark includes
25 motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures. In certain embodiments, amelioration of one or more of these symptoms or hallmarks result in improved motor function, reduction of alpha-synuclein aggregates, slowed neurodegeneration, slowed cognitive decline, reduced dementia, improved sleep, improved sense of smell, slowed autonomic failure, slowed ataxia, reduced hallucination, and/or reduced seizures.

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BRIEF DESCRIPTION OF THE DRAWINGS

Various aspects of the disclosure are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present disclosure will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the disclosure are utilized, and the
35 accompanying drawings below.

FIG. 1 illustrates a duration of action study using illustrative modified oligonucleotides described herein.

FIG. 2 illustrates tissue concentration of exemplary modified oligonucleotides described herein.

FIG. 3 illustrates ASO concentration using illustrative modified oligonucleotides described herein.

Detailed Description

It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive. Herein, the use of the singular includes the plural unless specifically stated otherwise. As used herein, the use of “or” means “and/or” unless stated otherwise. Furthermore, the use of the term “including” as well as other forms, such as “includes” and “included”, is not limiting. Also, terms such as “element” or “component” encompass both elements and components comprising one unit and elements and components that comprise more than one subunit, unless specifically stated otherwise.

The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in this application, including, but not limited to, patents, patent applications, articles, books, and treatises, are hereby expressly incorporated by reference for the portions of the document discussed herein, as well as in their entirety.

DEFINITIONS

Unless specific definitions are provided, the nomenclature used in connection with, and the procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art. Where permitted, all patents, applications, published applications and other publications and other data referred to throughout the disclosure are incorporated by reference herein in their entirety.

Unless otherwise indicated, the following terms have the following meanings:

As used herein, “2'-deoxynucleoside” means a nucleoside comprising a 2'-H(H) deoxyribosyl sugar moiety. In certain embodiments, a 2'-deoxynucleoside is a 2'-β-D-deoxynucleoside and comprises a 2'-β-D-deoxyribosyl sugar moiety, which has the β-D ribosyl configuration as found in naturally occurring deoxyribonucleic acids (DNA). In certain embodiments, a 2'-deoxynucleoside or a nucleoside comprising an unmodified 2'-deoxyribosyl sugar moiety may comprise a modified nucleobase or may comprise an RNA nucleobase (uracil).

As used herein, “2'-MOE” means a 2'-OCH₂CH₂OCH₃ group in place of the 2'-OH group of a ribosyl sugar moiety. A “2'-MOE sugar moiety” means a sugar moiety with a 2'-OCH₂CH₂OCH₃ group in place of the 2'-OH group of a ribosyl sugar moiety. Unless otherwise indicated, a 2'-MOE sugar moiety is in the β-D configuration. “MOE” means O-methoxyethyl.

As used herein, “2'-MOE nucleoside” or “2'-O(CH₂)₂OCH₃ nucleoside” means a nucleoside comprising a 2'-MOE sugar moiety (or 2'-OCH₂CH₂OCH₃ ribosyl sugar moiety).

As used herein, “2'-OMe” means a 2'-OCH₃ group in place of the 2'-OH group of a ribosyl sugar moiety. A “2'-O-methyl sugar moiety” means a sugar moiety with a 2'-OCH₃ group in place of the 2'-OH group of a ribosyl sugar moiety. Unless otherwise indicated, a 2'-OMe has the β-D ribosyl stereochemical configuration.

As used herein, “2'-OMe nucleoside” means a nucleoside comprising a 2'-OMe sugar moiety.

As used herein, “2'-F” means a 2'-fluoro group in place of the 2'-OH group of a furanosyl sugar moiety. A “2'-F sugar moiety” means a sugar moiety with a 2'-F group in place of the 2'-OH group of a furanosyl sugar moiety. Unless otherwise indicated, a 2'-F sugar moiety is in the β-D-ribose configuration.

As used herein, “2'-F nucleoside” means a nucleoside comprising a 2'-F modified sugar moiety.

As used herein, “2’-substituted nucleoside” means a nucleoside comprising a 2’-substituted furanosyl sugar moiety. As used herein, “2’-substituted” in reference to a sugar moiety means a sugar moiety comprising at least one 2’-substituent group other than H or OH.

As used herein, “5-methylcytosine” means a cytosine modified with a methyl group attached to the 5 position.
5 A 5-methylcytosine is a modified nucleobase.

As used herein, “abasic sugar moiety” means a sugar moiety that is not attached to a nucleobase. Such abasic sugar moieties are sometimes referred to in the art as “abasic nucleosides.”

As used herein, “administration” or “administering” means providing a pharmaceutical agent or composition to a subject.

10 As used herein, “ameliorate” in reference to a treatment means improvement in at least one symptom or hallmark relative to the same symptom or hallmark in the absence of the treatment. In certain embodiments, amelioration is the reduction in the severity or frequency of a symptom or hallmark or the delayed onset or slowing of progression in the severity or frequency of a symptom or hallmark. In certain embodiments, the symptom or hallmark is motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders,
15 hyposmia, autonomic failure, ataxia, hallucination, or seizures. The progression or severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

As used herein, “antisense activity” means any detectable and/or measurable change attributable to the hybridization of an antisense compound to its target nucleic acid. In certain embodiments, antisense activity is a decrease in the amount or expression of a target nucleic acid or protein encoded by such target nucleic acid compared to
20 target nucleic acid levels or target protein levels in the absence of the antisense compound.

As used herein, “antisense agent” means an antisense compound and optionally one or more additional features, such as a sense compound.

As used herein, “antisense compound” means an antisense oligonucleotide and optionally one or more additional features, such as a conjugate group.

25 As used herein, “sense compound” means a sense oligonucleotide and optionally one or more additional features, such as a conjugate group.

As used herein, “antisense oligonucleotide” means an oligonucleotide, including the oligonucleotide portion of an antisense compound, that is capable of hybridizing to a target nucleic acid and is capable of at least one antisense activity. Antisense oligonucleotides include but are not limited to antisense RNAi oligonucleotides and antisense RNase
30 H oligonucleotides.

As used herein, “sense oligonucleotide” means an oligonucleotide, including the oligonucleotide portion of a sense compound, that is capable of hybridizing to an antisense oligonucleotide. Sense oligonucleotides include, but are not limited to, sense RNAi oligonucleotides.

As used herein, “bicyclic nucleoside” or “BNA” means a nucleoside comprising a bicyclic sugar moiety.

35 As used herein, “bicyclic sugar” or “bicyclic sugar moiety” means a modified sugar moiety comprising two rings, wherein the second ring is formed via a bridge connecting two of the atoms in the first ring thereby forming a bicyclic structure. In certain embodiments, the first ring of the bicyclic sugar moiety is a furanosyl sugar moiety. In certain embodiments, the furanosyl sugar moiety is a ribosyl sugar moiety. In certain embodiments, the bicyclic sugar moiety does not comprise a furanosyl sugar moiety.

As used herein, “blunt” or “blunt ended” in reference to an oligomeric duplex formed by two oligonucleotides means that there are no terminal unpaired nucleotides (i.e. no overhanging nucleotides). One or both ends of a double-stranded RNAi agent can be blunt.

As used herein, “cell-targeting moiety” means a conjugate moiety or portion of a conjugate moiety that is capable of binding to a particular cell type or particular cell types.

As used herein, “cerebrospinal fluid” or “CSF” means the fluid filling the space around the brain and spinal cord. “Artificial cerebrospinal fluid” or “aCSF” means a prepared or manufactured fluid that has certain properties (e.g., osmolarity, pH, and/or electrolytes) similar to cerebrospinal fluid and is biocompatible with CSF.

As used herein, “chirally enriched” in reference to a population means a plurality of molecules of identical molecular formula, wherein the number or percentage of molecules within the population that contain a particular stereochemical configuration at a particular chiral center is greater than the number or percentage of molecules expected to contain the same particular stereochemical configuration at the same particular chiral center within the population if the particular chiral center were stereorandom as defined herein. Chirally enriched populations of molecules having multiple chiral centers within each molecule may contain one or more stereorandom chiral centers. In certain embodiments, the molecules are modified oligonucleotides. In certain embodiments, the molecules are oligomeric compounds comprising modified oligonucleotides. In certain embodiments, the chiral center is at the phosphorous atom of a phosphorothioate internucleoside linkage. In certain embodiments, the chiral center is at the phosphorous atom of a mesyl phosphoramidate internucleoside linkage.

As used herein, “cleavable moiety” means a bond or group of atoms that is cleaved upon administration to a subject, for example, inside a cell, a subject, or a human.

As used herein, “complementary” in reference to an oligonucleotide means that at least 70% of the nucleobases of the oligonucleotide or one or more portions thereof and the nucleobases of another nucleic acid or one or more portions thereof are capable of hydrogen bonding with one another when the nucleobase sequence of the oligonucleotide and the other nucleic acid are aligned in opposing directions. As used herein, “complementary nucleobases” means nucleobases that are capable of forming hydrogen bonds with one another. Complementary nucleobase pairs include adenine (A) and thymine (T), adenine (A) and uracil (U), cytosine (C) and guanine (G), 5-methylcytosine (^mC) and guanine (G). Certain modified nucleobases that pair with unmodified nucleobases or with other modified nucleobases are known in the art. For example, inosine can pair with adenosine, cytosine, or uracil. Complementary oligonucleotides and/or nucleic acids need not have nucleobase complementarity at each nucleoside. Rather, some mismatches are tolerated. As used herein, “fully complementary” or “100% complementary” in reference to an oligonucleotide, or a portion thereof, means that the oligonucleotide, or portion thereof, is complementary to another oligonucleotide or nucleic acid at each nucleobase of the shorter of the two oligonucleotides, or at each nucleoside if the oligonucleotides are the same length.

As used herein, “complementary region” in reference to an oligonucleotide is the range of nucleobases of the oligonucleotide that is complementary with a second oligonucleotide or target nucleic acid.

As used herein, “conjugate group” means a group of atoms directly attached to an oligonucleotide that confers at least one property to the resulting conjugated oligonucleotide. Conjugate groups comprise a conjugate moiety and a conjugate linker that attaches the conjugate moiety to the oligonucleotide.

As used herein, “conjugate linker” means a single bond or a group of atoms comprising at least one bond that connects a conjugate moiety to an oligonucleotide.

As used herein, “conjugate moiety” means a group of atoms that when covalently bound to a molecule modifies one or more properties of such molecule compared to the identical molecule lacking the conjugate moiety, wherein such properties include, but are not limited to pharmacodynamics, pharmacokinetics, stability, binding, absorption, tissue distribution, cellular distribution, cellular uptake, charge, and clearance.

As used herein, “contiguous” in the context of an oligonucleotide refers to nucleosides, nucleobases, sugar moieties, or internucleoside linkages that are immediately adjacent to each other. For example, “contiguous nucleobases” means nucleobases that are immediately adjacent to each other in a sequence.

As used herein, “constrained ethyl” or “cEt” or “cEt sugar moiety” means a β -D ribosyl bicyclic sugar moiety wherein the second ring of the bicyclic sugar is formed via a bridge connecting the 4'-carbon and the 2'-carbon of the β -D ribosyl sugar moiety, wherein the bridge has the formula 4'-CH(CH₃)-O-2', and wherein the methyl group of the bridge is in the *S* configuration.

As used herein, “cEt nucleoside” means a nucleoside comprising a cEt sugar moiety.

As used herein, “deoxy region” means a region of 5-12 contiguous nucleotides, wherein at least 70% of the nucleosides comprise a 2'-deoxy sugar moiety. In certain embodiments, each nucleoside is selected from a 2'- β -D-deoxynucleoside, a bicyclic nucleoside, and a 2'-substituted nucleoside. In certain embodiments, a deoxy region supports RNase H activity. In certain embodiments, a deoxy region is the gap or internal region of a gapmer.

As used herein, “diluent” means an ingredient in a composition that lacks pharmacological activity, but is pharmaceutically necessary or desirable. For example, the diluent in an injected composition can be a liquid, e.g., aCSF, PBS, or saline solution.

As used herein, “double-stranded” in reference to a region or an oligonucleotide means a duplex formed by complementary strands of nucleic acids (including, but not limited to oligonucleotides) hybridized to one another. In certain embodiments, the two strands of a double-stranded region are separate molecules. In certain embodiments, the two strands are regions of the same molecule that has folded onto itself (e.g., a hairpin structure).

As used herein, “duplex” or “duplex region” means the structure formed by two oligonucleotides or portions thereof that are hybridized to one another.

As used herein, “gapmer” means a modified oligonucleotide comprising an internal region having a plurality of nucleosides that support RNase H cleavage positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the “gap” and the external regions may be referred to as the “wings” or “wing segments.” In certain embodiments, the internal region is a deoxy region. The positions of the internal region or gap refer to the order of the nucleosides of the internal region and are counted starting from the 5'-end of the internal region. Unless otherwise indicated, “gapmer” refers to a sugar motif. In certain embodiments, each nucleoside of the gap is a 2'- β -D-deoxynucleoside. In certain embodiments, the gap comprises one 2'-substituted nucleoside at position 1, 2, 3, 4, or 5 of the gap, and the remainder of the nucleosides of the gap are 2'- β -D-deoxynucleosides. As used herein, the term “MOE gapmer” indicates a gapmer having a gap comprising 2'- β -D-deoxynucleosides and wings comprising 2'-MOE nucleosides. As used herein, the term “mixed wing gapmer” indicates a gapmer having wings comprising modified nucleosides comprising at least two different sugar modifications. Unless

otherwise indicated, a gapmer may comprise one or more modified internucleoside linkages and/or modified nucleobases and such modifications do not necessarily follow the gapmer pattern of the sugar modifications.

As used herein, "hotspot region" is a range of nucleobases on a target nucleic acid that is amenable to reduction of the amount or activity of the target nucleic acid by the action of an oligomeric agent, oligomeric compound, antisense compound, or antisense agent. Hotspot regions comprise at least one portion that is complementary to an active
5 antisense oligonucleotide.

As used herein, "hybridization" means the annealing of oligonucleotides and/or nucleic acids. While not limited to a particular mechanism, the most common mechanism of hybridization involves hydrogen bonding, which may be Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding, between complementary nucleobases. In certain
10 embodiments, complementary nucleic acid molecules include, but are not limited to, an antisense compound and a nucleic acid target. In certain embodiments, complementary nucleic acid molecules include, but are not limited to, an oligonucleotide and a nucleic acid target.

As used herein, "internucleoside linkage" means the covalent linkage between contiguous nucleosides in an oligonucleotide. As used herein, "modified internucleoside linkage" means any internucleoside linkage other than a
15 phosphodiester internucleoside linkage. "Phosphorothioate internucleoside linkage" or "PS internucleoside linkage" is a modified internucleoside linkage in which one of the non-bridging oxygen atoms of a phosphodiester internucleoside linkage is replaced with a sulfur atom.

As used herein, "inverted nucleoside" means a nucleotide having a 3' to 3' and/or 5' to 5' internucleoside linkage, as shown herein.

As used herein, "inverted sugar moiety" means the sugar moiety of an inverted nucleoside or an abasic sugar moiety having a 3' to 3' and/or 5' to 5' internucleoside linkage.
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As used herein, "linked nucleosides" are nucleosides that are connected in a contiguous sequence (i.e., no additional nucleosides are presented between those that are linked).

As used herein, "linker-nucleoside" means a nucleoside that links, either directly or indirectly, an
25 oligonucleotide to a conjugate moiety. Linker-nucleosides are located within the conjugate linker of an oligomeric compound. Linker-nucleosides are not considered part of the oligonucleotide portion of an oligomeric compound even if they are contiguous with the oligonucleotide.

As used herein, "mismatch" or "non-complementary" means a nucleobase of a first nucleic acid sequence that is not complementary with the corresponding nucleobase of a second nucleic acid sequence or target nucleic acid when
30 the first and second nucleic acid sequences are aligned in opposing directions.

As used herein, "motif" means the pattern of unmodified and/or modified sugar moieties, nucleobases, and/or internucleoside linkages, in an oligonucleotide.

As used herein, "non-bicyclic modified sugar moiety" means a modified sugar moiety that comprises a modification, such as a substituent, that does not form a bridge between two atoms of the sugar to form a second ring.

As used herein, "nucleobase" means an unmodified nucleobase or a modified nucleobase. As used herein an
35 "unmodified nucleobase" is adenine (A), thymine (T), cytosine (C), uracil (U), or guanine (G). As used herein, a "modified nucleobase" is a group of atoms other than unmodified A, T, C, U, or G capable of pairing with at least one unmodified nucleobase. A "5-methylcytosine" is a modified nucleobase. A universal base is a modified nucleobase that can pair with any one of the five unmodified nucleobases.

As used herein, “nucleobase sequence” means the order of contiguous nucleobases in a nucleic acid or oligonucleotide independent of any sugar or internucleoside linkage modification.

As used herein, “the nucleobase sequence of” a reference SEQ ID NO, refers only to the nucleobase sequence provided in such SEQ ID NO and therefore, unless otherwise indicated, includes compounds wherein each sugar moiety and each internucleoside linkage, independently, may be modified or unmodified, irrespective of the presence or absence of modifications, indicated in the referenced SEQ ID NO.

As used herein, “nucleoside” means a compound, or fragment of a compound, comprising a nucleobase and a sugar moiety. The nucleobase and sugar moiety are each, independently, unmodified or modified.

As used herein, “modified nucleoside” means a nucleoside comprising a modified nucleobase and/or a modified sugar moiety. “Linked nucleosides” are nucleosides that are connected in a contiguous sequence (i.e., no additional nucleosides are presented between those that are linked).

As used herein, “oligomeric agent” means an oligomeric compound and optionally one or more additional features, such as a second oligomeric compound. An oligomeric agent may be a single-stranded oligomeric compound or may be an oligomeric duplex formed by two complementary oligomeric compounds.

As used herein, “oligomeric compound” means an oligonucleotide and optionally one or more additional features, such as a conjugate group or terminal group. An oligomeric compound may be paired with a second oligomeric compound that is complementary to the first oligomeric compound or may be unpaired. A “single-stranded oligomeric compound” is an unpaired oligomeric compound.

The term “oligomeric duplex” means a duplex formed by two oligomeric compounds having complementary nucleobase sequences. Each oligomeric compound of an oligomeric duplex may be referred to as a “duplexed oligomeric compound.”

As used herein, “oligonucleotide” means a polymer of linked nucleosides connected via internucleoside linkages, wherein each nucleoside and internucleoside linkage may be modified or unmodified. Unless otherwise indicated, oligonucleotides consist of 8-50 linked nucleosides.

As used herein, “modified oligonucleotide” means an oligonucleotide, wherein at least one nucleoside or internucleoside linkage is modified. As used herein, “unmodified oligonucleotide” means an oligonucleotide that does not comprise any nucleoside modifications or internucleoside modifications. An oligonucleotide may be paired with a second oligonucleotide that is complementary to the oligonucleotide or it may be unpaired. A “single-stranded oligonucleotide” is an unpaired oligonucleotide. A “double-stranded oligonucleotide” is an oligonucleotide that is paired with a second oligonucleotide.

As used herein, “pharmaceutically acceptable carrier or diluent” means any substance suitable for use in administering to a subject. Certain such carriers enable pharmaceutical compositions to be formulated as, for example, tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspension and lozenges for the oral ingestion by a subject. In certain embodiments, a pharmaceutically acceptable carrier or diluent is sterile water, sterile saline, sterile buffer solution or sterile artificial cerebrospinal fluid.

As used herein “pharmaceutically acceptable salts” means physiologically and pharmaceutically acceptable salts of compounds. Pharmaceutically acceptable salts retain the desired biological activity of the parent compound and do not impart undesired toxicological effects thereto.

As used herein “pharmaceutical composition” means a mixture of substances suitable for administering to a subject. For example, a pharmaceutical composition may comprise an oligomeric compound and a sterile aqueous solution. In certain embodiments, a pharmaceutical composition shows activity in free uptake assay in certain cell lines.

As used herein “prodrug” means an inactive or less active form of a compound which, when administered to a subject, is metabolized to form the active, or more active, compound. In certain embodiments, a prodrug comprises a cell-targeting moiety and at least one active compound.

As used herein, “reducing or inhibiting the amount or activity” refers to a reduction or blockade of the transcriptional expression or activity relative to the transcriptional expression or activity in an untreated or control sample and does not necessarily indicate a total elimination of transcriptional expression or activity.

As used herein, “RNA” means an RNA transcript and includes pre-mRNA and mature mRNA unless otherwise specified.

As used herein, “RNAi agent” means an antisense agent that acts, at least in part, through RISC or Ago2 to modulate a target nucleic acid and/or protein encoded by a target nucleic acid. RNAi agents include, but are not limited to double-stranded siRNA, single-stranded RNA (ssRNAi), and microRNA, including microRNA mimics. RNAi agents may comprise conjugate groups and/or terminal groups. In certain embodiments, an RNAi agent modulates the amount, activity, and/or splicing of a target nucleic acid. The term RNAi agent excludes antisense agents that act principally through RNase H.

As used herein, “RNase H agent” means an antisense agent that acts through RNase H to modulate a target nucleic acid and/or protein encoded by a target nucleic acid. In certain embodiments, RNase H agents are single-stranded. In certain embodiments, RNase H agents are double-stranded. RNase H agents may comprise conjugate groups and/or terminal groups. In certain embodiments, an RNase H agent modulates the amount and/or activity of a target nucleic acid. The term RNase H agent excludes antisense agents that act principally through RISC/Ago2.

As used herein, “antisense RNase H oligonucleotide” means an oligonucleotide comprising a region that is complementary to a target sequence, and which includes at least one chemical modification suitable for RNase H-mediated nucleic acid reduction.

As used herein, “antisense RNAi oligonucleotide” means an oligonucleotide comprising a region that is complementary to a target sequence, and which includes at least one chemical modification suitable for RNAi-mediated nucleic acid reduction.

As used herein, “self-complementary” in reference to an oligonucleotide means an oligonucleotide that at least partially hybridizes to itself.

As used herein, “single-stranded” means a nucleic acid (including but not limited to an oligonucleotide) that is unpaired and is not part of a duplex. Single-stranded compounds are capable of hybridizing with complementary nucleic acids to form duplexes, at which point they are no longer single-stranded.

As used herein, “stabilized phosphate group” means a 5'-phosphate analog that is metabolically more stable than a 5'-phosphate as naturally occurs on DNA or RNA.

As used herein, “standard *in vitro* assay” means the assay described in Example 1, 2, 3, 4, 5, 6, 7, or 8, and reasonable variations thereof.

As used herein, “standard *in vivo* assay” means the assay described in Example 10, 11, 12, 13, 14, or 15, and reasonable variations thereof.

As used herein, "stereorandom" or "stereorandom chiral center" in the context of a population of molecules of identical molecular formula means a chiral center that is not controlled during synthesis, or enriched following synthesis, for a particular absolute stereochemical configuration. The stereochemical configuration of a chiral center is random when it is the result of a synthetic method that is not designed to control the stereochemical configuration. For example, in a population of molecules comprising a stereorandom chiral center, the number of molecules having the (*S*) configuration of the stereorandom chiral center may be the same as the number of molecules having the (*R*) configuration of the stereorandom chiral center ("racemic"). The stereochemical configuration of a chiral center is random when it is the result of a synthetic method that is not designed to control the stereochemical configuration. In certain embodiments, the stereorandom chiral center is at the phosphorous atom of a stereorandom phosphorothioate or mesyl phosphoramidate internucleoside linkage.

As used herein, "subject" means a human or non-human animal. In certain embodiments, the subject is a human.

As used herein, "sugar moiety" means an unmodified sugar moiety or a modified sugar moiety. As used herein, "unmodified sugar moiety" means a 2'-OH(H) β -D-ribosyl sugar moiety, as found in RNA (an "unmodified RNA sugar moiety"), or a 2'-H(H) β -D-deoxyribosyl sugar moiety, as found in DNA (an "unmodified DNA sugar moiety"). Unmodified sugar moieties have one hydrogen at each of the 1', 3', and 4' positions, an oxygen at the 3' position, and two hydrogens at the 5' position. As used herein, "modified sugar moiety" or "modified sugar" means a modified furanosyl sugar moiety or a sugar surrogate.

As used herein, "sugar surrogate" means a modified sugar moiety having other than a furanosyl moiety that can link a nucleobase to another group, such as an internucleoside linkage, conjugate group, or terminal group in an oligonucleotide. Modified nucleosides comprising sugar surrogates can be incorporated into one or more positions within an oligonucleotide and such oligonucleotides are capable of hybridizing to complementary oligomeric compounds or target nucleic acids.

As used herein, "symptom or hallmark" means any physical feature or test result that indicates the existence or extent of a disease or disorder. In certain embodiments, a symptom is apparent to a subject or to a medical professional examining or testing said subject. In certain embodiments, a hallmark is apparent upon invasive diagnostic testing, including, but not limited to, post-mortem tests. In certain embodiments, symptoms and hallmarks include motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.

As used herein, "target nucleic acid" and "target RNA" mean a nucleic acid that an antisense compound is designed to affect. Target RNA means an RNA transcript and includes pre-mRNA and mature mRNA unless otherwise specified.

As used herein, "target region" means a portion of a target nucleic acid to which an oligomeric compound is designed to hybridize.

As used herein, "terminal group" means a chemical group or group of atoms that is covalently linked to a terminus of an oligonucleotide.

As used herein, "treating" means improving a subject's disease or condition by administering an oligomeric agent or oligomeric compound described herein. In certain embodiments, treating a subject improves a symptom relative to the same symptom in the absence of the treatment. In certain embodiments, treatment reduces in the severity or

frequency of a symptom, or delays the onset of a symptom, slows the progression of a symptom, or slows the severity or frequency of a symptom.

As used herein, “therapeutically effective amount” means an amount of a pharmaceutical agent or composition that provides a therapeutic benefit to a subject. For example, a therapeutically effective amount improves a symptom of a disease.

CERTAIN EMBODIMENTS

The present disclosure provides the following non-limiting numbered embodiments:

10 Embodiment 1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of a SNCA nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar and a modified internucleoside linkage.

15 Embodiment 2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 13-3334, wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

20 Embodiment 3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases complementary to:

an equal length portion of nucleobases 16,692-16,716 of SEQ ID NO: 1 or nucleobases 18,758-18,782 of SEQ ID NO: 2;

an equal length portion of nucleobases 18,568-18,593 of SEQ ID NO: 1 or nucleobases 20,634-20,659 of SEQ ID NO: 2;

25 an equal length portion of nucleobases 18,621-18,649 of SEQ ID NO: 1 or nucleobases 20,687-20,715 of SEQ ID NO: 2;

an equal length portion of nucleobases 18,721-18,752 of SEQ ID NO: 1 or nucleobases 20,787-20,818 of SEQ ID NO: 2;

30 an equal length portion of nucleobases 19,423-19,443 of SEQ ID NO: 1 or nucleobases 21,489-21,509 of SEQ ID NO: 2;

an equal length portion of nucleobases 19,555-19,575 of SEQ ID NO: 1 or nucleobases 21,621-21,641 of SEQ ID NO: 2;

an equal length portion of nucleobases 21,457-21,501 of SEQ ID NO: 1 or nucleobases 23,523-23,567 of SEQ ID NO: 2;

35 an equal length portion of nucleobases 22,008-22,030 of SEQ ID NO: 1 or nucleobases 24,074-24,096 of SEQ ID NO: 2;

an equal length portion of nucleobases 22,507-22,529 of SEQ ID NO: 1 or nucleobases 24,573-24,595 of SEQ ID NO: 2;

- an equal length portion of nucleobases 22,614-22,637 of SEQ ID NO: 1 or nucleobases 24,680-24,703 of SEQ ID NO: 2;
- an equal length portion of nucleobases 25,049-25,090 of SEQ ID NO: 1 or nucleobases 27,115-27,156 of SEQ ID NO: 2;
- 5 an equal length portion of nucleobases 26,367-26,388 of SEQ ID NO: 1 or nucleobases 28,433-28,454 of SEQ ID NO: 2;
- an equal length portion of nucleobases 26,508-26,531 of SEQ ID NO: 1 or nucleobases 28,574-28,597 of SEQ ID NO: 2;
- 10 an equal length portion of nucleobases 30,207-30,226 of SEQ ID NO: 1 or nucleobases 32,273-32,292 of SEQ ID NO: 2;
- an equal length portion of nucleobases 31,412-31,438 of SEQ ID NO: 1 or nucleobases 33,478-33,504 of SEQ ID NO: 2;
- an equal length portion of nucleobases 33,027-33,057 of SEQ ID NO: 1 or nucleobases 35,093-35,123 of SEQ ID NO: 2; or
- 15 an equal length portion of nucleobases 48,460-48,489 of SEQ ID NO: 1 or nucleobases 50,526-50,555 of SEQ ID NO: 2;
- wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.
- Embodiment 4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked
- 20 nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of:
- SEQ ID NO: 78, 2564, 2697, 2747, 2789, 2936, 3063, 3081, 3142, 3189, or 3271;
- SEQ ID NO: 206, 231, 270, 316, 2486, 2558, 3041, 3076, 3137, 3184, or 3266;
- SEQ ID NO: 64, 128, 289, 921, 2744, 2853, 2922, 3031, 3057, 3099, 3123, 3132, 3160, 3207, 3231,
- 25 3289, or 3313;
- SEQ ID NO: 227, 427, 545, 1214, 1279, 1385, 1401, 1476, 1616, 3048, 3115, 3176, or 3305;
- SEQ ID NO: 203, 285, 1974, 2044, 2949, 3021, 3090, 3151, 3198, or 3280;
- SEQ ID NO: 205, 2594, 2686, 3028, 3097, 3158, 3205, or 3287;
- SEQ ID NO: 214, 247, 865, 1887, 1948, 3067, 3085, 3146, 3193, or 3275;
- 30 SEQ ID NO: 167, 208, 248, 304, 1930, 3054, 3120, 3129, 3228, or 3310;
- SEQ ID NO: 196, 1814, 1909, 3042, 3109, 3170, 3217, or 3299;
- SEQ ID NO: 171, 207, 245, 489, 2390, 3053, 3119, 3128, 3227, or 3309;
- SEQ ID NO: 24, 133, 199, 228, 230, 276, 314, 946, 2759, 2818, 2873, 3069, 3087, 3148, 3195, or
- 3277;
- 35 SEQ ID NO: 168, 193, 236, 313, 2446, 3049, 3116, 3177, 3224, or 3306;
- SEQ ID NO: 210, 223, 272, 273, 274, 1026, 1143, 3020, 3089, 3150, 3197, or 3279;
- SEQ ID NO: 287, 964, 1040, 1154, 3050, 3117, 3178, 3225, or 3307;
- SEQ ID NO: 119, 980, 1085, 1166, 3051, 3118, 3127, 3226, or 3308;
- SEQ ID NO: 194, 277, 1113, 1185, 1309, 3024, 3093, 3154, 3201, or 3283; or

SEQ ID NO: 310, 803, 919, 1582, 1674, 3032, 3032, 3032, 3100, 3161, 3208, 3290, or 3290;

wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

5 Embodiment 5. The oligomeric compound of any of embodiments 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 85%, at least 90%, at least 95%, or 100% complementary to the nucleobase sequence of any one of SEQ ID NOs: 1-9 when measured across the entire nucleobase sequence of the modified oligonucleotide.

10 Embodiment 6. The oligomeric compound of any of embodiments 1-5, wherein the modified oligonucleotide consists of 12 to 20, 12 to 25, 12 to 30, 12 to 50, 13 to 20, 13 to 25, 13 to 30, 13 to 50, 14 to 20, 14 to 25, 14 to 30, 14 to 50, 15 to 20, 15 to 25, 15 to 30, 15 to 50, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 16 to 50, 17 to 20, 17 to 25, 17 to 30, 17 to 50, 18 to 20, 18 to 25, 18 to 30, 18 to 50, 19 to 20, 19 to 25, 19 to 30, 19 to 50, 20 to 25, 20 to 30, or 20 to 50 linked nucleosides.

Embodiment 7. The oligomeric compound of any of embodiments 1-6, wherein at least one nucleoside of the modified oligonucleotide is a modified nucleoside.

15 Embodiment 8. The oligomeric compound of embodiment 7, wherein the modified nucleoside comprises a modified sugar moiety.

Embodiment 9. The oligomeric compound of embodiment 8, wherein the modified sugar moiety comprises a bicyclic sugar moiety.

20 Embodiment 10. The oligomeric compound of embodiment 9, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.

Embodiment 11. The oligomeric compound of any of embodiments 7-10, wherein the modified nucleoside comprises a non-bicyclic modified sugar moiety.

25 Embodiment 12. The oligomeric compound of embodiment 11, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, a 2'-β-D-deoxyxylosyl sugar moiety, or a 2'-α-L-deoxyribosyl sugar moiety.

Embodiment 13. The oligomeric compound of any of embodiments 7-12, wherein the modified nucleoside comprises a sugar surrogate.

30 Embodiment 14. The oligomeric compound of embodiment 13, wherein the sugar surrogate is any of morpholino, modified morpholino, glycol nucleic acid (GNA), six-membered tetrahydropyran (THP), and F-hexitol nucleic acid (F-HNA).

Embodiment 15. The oligomeric compound of any of embodiments 1-14, wherein the modified oligonucleotide is a gapmer.

Embodiment 16. The oligomeric compound of any of embodiments 1-15, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

35 Embodiment 17. The oligomeric compound of embodiment 16, wherein at least one internucleoside linkage is a phosphodiester internucleoside linkage.

Embodiment 18. The oligomeric compound of embodiment 16 or embodiment 17, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 19. The oligomeric compound of any of embodiments 16-18, wherein at least one modified internucleoside linkage is a mesyl phosphoramidate internucleoside linkage.

Embodiment 20. The oligomeric compound of any of embodiments 16-19, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, and a mesyl phosphoramidate internucleoside linkage.

Embodiment 21. The oligomeric compound of any of embodiments 16, 18, or 19, wherein each internucleoside linkage is independently selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage.

Embodiment 22. The oligomeric compound of any of embodiments 16-18, wherein each internucleoside
10 linkage is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.

Embodiment 23. The oligomeric compound of any of embodiments 16-22, wherein at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, or 19 internucleoside linkages of the modified oligonucleotide are phosphorothioate internucleoside linkages.

Embodiment 24. The oligomeric compound of any of embodiments 16-21, wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 internucleoside linkages of the modified oligonucleotide are mesyl phosphoramidate internucleoside linkages.

[illegible]

Embodiment 26. The oligomeric compound of any of embodiments 1-25, wherein at least one nucleoside of the modified oligonucleotide comprises a modified nucleobase.

Embodiment 27. The oligomeric compound of embodiment 26, wherein the modified nucleobase is a 5-methylcytosine.

Embodiment 28. The oligomeric compound of embodiment 27, wherein each cytosine is a 5-methylcytosine.

Embodiment 29. The oligomeric compound of any of embodiments 1-28, wherein each nucleoside of the modified oligonucleotide is unmodified adenine, unmodified guanine, unmodified thymine, unmodified cytosine, or 5-methylcytosine.

Embodiment 30. The oligomeric compound of any of embodiments 1-29, wherein the modified oligonucleotide comprises a deoxy region.

Embodiment 31. The oligomeric compound of embodiment 30, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.

Embodiment 32. The oligomeric compound of embodiment 30 or embodiment 31, wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.

Embodiment 33. The oligomeric compound of any of embodiments 30-32, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.

Embodiment 34. The oligomeric compound of any of embodiments 30-33, wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein at least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 35. The oligomeric compound of embodiment 34, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.

Embodiment 36. The oligomeric compound of embodiment 34 or embodiment 35, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 37. The oligomeric compound of any of embodiments 1-36, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22 or 18-20 linked nucleosides.

Embodiment 38. The oligomeric compound of any of embodiments 1-37, wherein the modified oligonucleotide consists of 20 linked nucleosides.

Embodiment 39. The oligomeric compound of any of embodiments 1-38, wherein the modified oligonucleotide comprises:

a 5'-region consisting of 1-6 linked 5'-region nucleosides;
a central region consisting of 6-10 linked central region nucleosides; and
a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.

Embodiment 40. The oligomeric compound of any of embodiments 1-39, wherein the modified oligonucleotide has a sugar motif comprising:

a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

Embodiment 41. The oligomeric compound of embodiment 40, wherein the modified oligonucleotide has
5 a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and
each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

Embodiment 42. The oligomeric compound of any of embodiments 1-39, wherein the modified oligonucleotide
10 has a sugar motif comprising:
a 5'-region consisting of 6 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 4 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and
15 each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

Embodiment 43. The oligomeric compound of embodiment 42, wherein the modified oligonucleotide has
a 5'-region consisting of 6 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 4 linked 3'-region nucleosides; wherein
20 each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and
each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

Embodiment 44. The oligomeric compound of any of embodiments 1-43, consisting of the modified oligonucleotide.

Embodiment 45. The oligomeric compound of any of embodiments 1-43, wherein the oligomeric compound
25 comprises a conjugate group.

Embodiment 46. The oligomeric compound of embodiment 45, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

Embodiment 47. The oligomeric compound of embodiment 46, wherein the conjugate linker is a phosphodiester linker.

Embodiment 48. The oligomeric compound of embodiment 46, wherein the conjugate linker consists of a
30 single bond.

Embodiment 49. The oligomeric compound of any of embodiments 46 - 48, wherein the conjugate linker is cleavable.

Embodiment 50. The oligomeric compound of any of embodiments 46, 47, or 49, wherein the conjugate linker
35 comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the modified oligonucleotide, or to another linker-nucleoside by a phosphodiester bond.

Embodiment 51. The oligomeric compound of any of embodiments 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

Embodiment 52. The oligomeric compound of any of embodiments 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 53. The oligomeric compound of any of embodiments 1-49 or 51-52, wherein the oligomeric compound does not comprise linker-nucleosides.

5 Embodiment 54. The oligomeric compound of any of embodiments 1-53, comprising a terminal group.

Embodiment 55. The oligomeric compound of embodiment 54, wherein the terminal group is an abasic sugar moiety.

Embodiment 56. The oligomeric compound of any of embodiments 1-55, wherein the oligomeric compound is an RNase H agent.

10 Embodiment 57. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}^m C_{es} A_{es} G_{es} A_{es} T_{dz} A_{dz} T_{dz} T_{ds} T_{ds} T_{ds} G_{ds} T_{ds} T_{ds}^m C_{es} T_{es} G_{es}^m C_{es}^m C_e$ (SEQ ID NO: 3335), wherein:

A = an adenine nucleobase,

$^m C$ = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

15 T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

z = a mesyl phosphoramidate internucleoside linkage; and

20 wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

Embodiment 58. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}^m C_{es} G_{eo} A_{eo}^m C_{es} A_{dz} T_{ds} T_{ds} T_{ds}^m C_{ds} T_{ds} T_{dz} G_{ds}^m C_{ds} T_{es} T_{eo}^m C_{es} T_{es} T_e$ (SEQ ID NO: 3336), wherein:

A = an adenine nucleobase,

$^m C$ = a 5-methylcytosine nucleobase,

25 G = a guanine nucleobase,

T = a thymine nucleobase,

c = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage,

30 z = a mesyl phosphoramidate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

Embodiment 59. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}^m C_{es} A_{es} G_{es} A_{es} T_{dz} A_{dz} T_{ds} T_{ds} T_{ds} T_{dz} G_{dz} T_{ds} T_{ds}^m C_{es} T_{es} G_{es}^m C_{es}^m C_e$ (SEQ ID NO: 3337), wherein:

35 A = an adenine nucleobase,

$^m C$ = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribose sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

5 Embodiment 60. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: $A_{es}T_{eo}^mC_{eo}A_{eo}^mC_{eo}G_{eo}A_{ds}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{ds}G_{eo}^mC_{es}^mC_{es}T_e$ (SEQ ID NO: 3338), wherein:

A = an adenine nucleobase,
 mC = a 5-methylcytosine nucleobase,

10 G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

15 wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

Embodiment 61. The oligomeric compound of any of embodiments 57-60, wherein the modified oligonucleotide is a pharmaceutically acceptable salt.

Embodiment 62. The oligomeric compound of embodiment 61, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

20 Embodiment 63. The oligomeric compound of any of embodiments 1-62, wherein the oligomeric compound is a singled-stranded oligomeric compound.

Embodiment 64. An oligomeric compound according to the following chemical notation:

$N^1_{es}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{dz}T_{dz}T_{ds}T_{ds}T_{ds}G_{ds}T_{ds}T_{ds}^mC_{es}T_{es}G_{es}^mC_{es}N^2_e$ (SEQ ID NO: 3346), wherein:

A = an adenine nucleobase,

25 mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,

30 N^2 = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^2 is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

35 z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

Embodiment 65. An oligomeric compound according to the following chemical notation:

$N^1_{es}^mC_{es}G_{eo}A_{eo}^mC_{es}A_{dz}T_{ds}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{ds}G_{ds}^mC_{ds}T_{eo}^mC_{es}T_{es}N^3_e$ (SEQ ID NO: 3347), wherein:

A = an adenine nucleobase,

mC = a 5-methylcytosine nucleobase.

G = a guanine nucleobase.

T = a thymine nucleobase.

5 N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,

N^3 = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^3 is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety.

10 s = a phosphorothioate internucleoside linkage.

z = a mesyl phosphoramidate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

Embodiment 66. An oligomeric compound according to the following chemical notation:

15 $N^1_{es}{}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{ds}T_{ds}T_{ds}T_{dz}G_{dz}T_{ds}T_{ds}{}^mC_{es}T_{es}G_{es}{}^mC_{es}N^2_e$ (SEQ ID NO: 3348), wherein:

A = an adenine nucleobase,

mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

20 N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,

N^2 = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^2 is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

25 d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

Embodiment 67. An oligomeric compound according to the following chemical notation:

30 $N^1_{es}T_{eo}{}^mC_{eo}A_{eo}{}^mC_{eo}G_{eo}A_{ds}{}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}{}^mC_{ds}T_{ds}T_{ds}G_{eo}{}^mC_{es}{}^mC_{es}N^3_e$ (SEQ ID NO: 3349), wherein:

A = an adenine nucleobase,

mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

35 N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,

N^3 = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^3 is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

5 Embodiment 68. The oligomeric compound of any of embodiments 64-67, wherein N¹ is an adenine nucleobase.

Embodiment 69. The oligomeric compound of any of embodiments 64-67, wherein N¹ is an unmodified adenine.

Embodiment 70. The oligomeric compound of any of embodiments 64-67, wherein N¹ is a modified adenine.

10 Embodiment 71. The oligomeric compound of any of embodiments 64-67, wherein N¹ is a hypoxanthine.

Embodiment 72. The oligomeric compound of any of embodiments 64-67, wherein N¹ is an abasic sugar moiety.

Embodiment 73. The oligomeric compound of any of embodiments 64-67, wherein N¹ is a terminal group.

Embodiment 74. The oligomeric compound of any of embodiments 64-67, wherein N¹ is absent.

15 Embodiment 75. The oligomeric compound of any of embodiments 64-74, wherein N² is a modified cytosine.

Embodiment 76. The oligomeric compound of any of embodiments 64-74, wherein N² is 5-methylcytosine.

Embodiment 77. The oligomeric compound of any of embodiments 64-74, wherein N² is an unmodified cytosine.

20 Embodiment 78. The oligomeric compound of any of embodiments 64-74, wherein N² is an abasic sugar moiety.

Embodiment 79. The oligomeric compound of any of embodiments 64-74, wherein N² is a terminal group.

Embodiment 80. The oligomeric compound of any of embodiments 64-74, wherein N² is absent.

Embodiment 81. The oligomeric compound of any of embodiments 64-74, wherein N³ is a modified thymine.

25 Embodiment 82. The oligomeric compound of any of embodiments 64-74, wherein N³ is an unmodified thymine.

Embodiment 83. The oligomeric compound of any of embodiments 64-74, wherein N³ is an abasic sugar moiety.

Embodiment 84. The oligomeric compound of any of embodiments 64-74, wherein N³ is a terminal group.

Embodiment 85. The oligomeric compound of any of embodiments 64-74, wherein N³ is absent.

30 Embodiment 86. The oligomeric compound of any of embodiments 64-80, wherein N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

Embodiment 87. The oligomeric compound of any of embodiments 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is a modified cytosine.

35 Embodiment 88. The oligomeric compound of any of embodiments 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is an abasic sugar moiety.

Embodiment 89. The oligomeric compound of any of embodiments 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is a terminal group.

Embodiment 90. The oligomeric compound of any of embodiments 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is absent.

Embodiment 91. The oligomeric compound of any of embodiments 64-80, wherein N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

Embodiment 92. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a modified adenine and N² is a modified cytosine.

5 Embodiment 93. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a modified adenine and N² is 5-methylcytosine.

Embodiment 94. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a modified adenine and N² is an abasic sugar moiety.

10 Embodiment 95. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a modified adenine and N² is a terminal group.

Embodiment 96. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a modified adenine and N² is absent.

Embodiment 97. The oligomeric compound of any of embodiments 64-80 or 91, wherein N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

15 Embodiment 98. The oligomeric compound of any of embodiments 64-80 or 97, wherein N¹ is a hypoxanthine and N² is a modified cytosine.

Embodiment 99. The oligomeric compound of any of embodiments 64-80 or 97, wherein N¹ is a hypoxanthine and N² is 5-methylcytosine.

20 Embodiment 100. The oligomeric compound of any of embodiments 64-80 or 97, wherein N¹ is a hypoxanthine and N² is an abasic sugar moiety.

Embodiment 101. The oligomeric compound of any of embodiments 64-80 or 97, wherein N¹ is a hypoxanthine and N² is a terminal group.

Embodiment 102. The oligomeric compound of any of embodiments 64-80 or 97, wherein N¹ is a hypoxanthine and N² is absent.

25 Embodiment 103. The oligomeric compound of any of embodiments 64-80, wherein N¹ is an abasic sugar moiety and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

Embodiment 104. The oligomeric compound of any of embodiments 64-80, wherein N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

30 Embodiment 105. The oligomeric compound of any of embodiments 64-80, wherein N¹ is absent and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.

Embodiment 106. The oligomeric compound of any of embodiments 64-80, wherein N¹ is absent and N² is absent.

Embodiment 107. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

35 Embodiment 108. The oligomeric compound of any of embodiments 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a thymine nucleobase.

Embodiment 109. The oligomeric compound of any of embodiments 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a modified thymine.

Embodiment 110. The oligomeric compound of any of embodiments 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is an abasic sugar moiety.

Embodiment 111. The oligomeric compound of any of embodiments 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a terminal group.

5 Embodiment 112. The oligomeric compound of any of embodiments 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is absent.

Embodiment 113. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is a modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

10 Embodiment 114. The oligomeric compound of any of embodiments 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is an unmodified thymine.

Embodiment 115. The oligomeric compound of any of embodiments 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is an abasic sugar moiety.

Embodiment 116. The oligomeric compound of any of embodiments 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is a terminal group.

15 Embodiment 117. The oligomeric compound of any of embodiments 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is absent.

Embodiment 118. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is a hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

20 Embodiment 119. The oligomeric compound of any of embodiments 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is an unmodified thymine.

Embodiment 120. The oligomeric compound of any of embodiments 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is an abasic sugar moiety.

25 Embodiment 121. The oligomeric compound of any of embodiments 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is a terminal group.

Embodiment 122. The oligomeric compound of any of embodiments 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is absent.

Embodiment 123. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is an abasic sugar moiety and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

30 Embodiment 124. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

Embodiment 125. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is absent and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.

35 Embodiment 126. The oligomeric compound of any of embodiments 64-74 or 81-85, wherein N¹ is absent and N³ is absent.

Embodiment 127. The oligomeric compound of any of embodiments 64-126, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

Embodiment 128. The oligomeric compound of embodiment 127, wherein the conjugate linker is a phosphodiester linker.

Embodiment 129. The oligomeric compound of embodiment 127, wherein the conjugate linker consists of a single bond.

Embodiment 130. The oligomeric compound of any of embodiments 127-129, wherein the conjugate linker is cleavable.

5 Embodiment 131. The oligomeric compound of any of embodiments 127, 128, or 130, wherein the conjugate linker comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the oligomeric compound, or to another linker-nucleoside by a phosphodiester bond.

Embodiment 132. The oligomeric compound of any of embodiments 64-131, wherein the conjugate group is attached to the oligomeric compound at the 5'-end of the oligomeric compound.

10 Embodiment 133. The oligomeric compound of any of embodiments 64-131, wherein the conjugate group is attached to the oligomeric compound at the 3'-end of the oligomeric compound.

Embodiment 134. The oligomeric compound of any of embodiments 64-133, wherein the oligomeric compound is a pharmaceutically acceptable salt.

15 Embodiment 135. The oligomeric compound of embodiment 133, wherein the pharmaceutically acceptable salt comprises one or more cations selected from sodium, potassium, calcium, and magnesium.

Embodiment 136. An oligomeric duplex, comprising a first oligomeric compound and a second oligomeric compound comprising a second modified oligonucleotide, wherein the first oligomeric compound is an oligomeric compound of any of embodiments 1-135.

20 Embodiment 137. The oligomeric duplex of embodiment 136, wherein the second modified oligonucleotide consists of 12 to 50 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 8 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

Embodiment 138. The oligomeric duplex of embodiment 136 or embodiment 137, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.

25 Embodiment 139. The oligomeric duplex of embodiment 138, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.

Embodiment 140. The oligomeric duplex of any of embodiments 136-139, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.

30 Embodiment 141. The oligomeric duplex of embodiment 140, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.

Embodiment 142. The oligomeric duplex of embodiment 141, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.

Embodiment 143. The oligomeric duplex of embodiment 140, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.

35 Embodiment 144. The oligomeric duplex of embodiment 143, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-F modified sugar moiety, or 2'-OMe modified sugar moiety.

Embodiment 145. The oligomeric duplex of any of embodiments 136-144, wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage.

Embodiment 146. The oligomeric duplex of embodiment 145, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

Embodiment 147. The oligomeric duplex of any of embodiments 136-146, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage.

5 Embodiment 148. The oligomeric duplex of any of embodiments 145-147, wherein at least one internucleoside linkage of the second modified oligonucleotide is a mesyl phosphoramidate internucleoside linkage.

Embodiment 149. The oligomeric duplex of any of embodiments 136-148, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, or a mesyl phosphoramidate internucleoside linkage.

10 Embodiment 150. The oligomeric duplex of any of embodiments 136-149, wherein the second modified oligonucleotide comprises at least one modified nucleobase.

Embodiment 151. The oligomeric duplex of embodiment 150, wherein the at least one modified nucleobase of the second modified oligonucleotide is 5-methylcytosine.

15 Embodiment 152. The oligomeric duplex of any of embodiments 136-151, wherein the second modified oligonucleotide comprises a conjugate group.

Embodiment 153. The oligomeric duplex of embodiment 152, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

Embodiment 154. The oligomeric duplex of embodiment 153, wherein the conjugate linker consists of a single bond.

20 Embodiment 155. The oligomeric duplex of embodiment 153 or embodiment 154, wherein the conjugate linker is cleavable.

Embodiment 156. The oligomeric duplex of embodiment 153 or embodiment 155, wherein the conjugate linker comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the modified oligonucleotide, or to another linker-nucleoside by a phosphodiester bond.

25 Embodiment 157. The oligomeric duplex of any of embodiments 153-156, wherein the conjugate linker is a phosphodiester linker.

Embodiment 158. The oligomeric duplex of any of embodiments 152-157, wherein the conjugate group is attached to the 5'-end of the second modified oligonucleotide.

30 Embodiment 159. The oligomeric duplex of any of embodiments 152-157, wherein the conjugate group is attached to the 3'-end of the second modified oligonucleotide.

Embodiment 160. The oligomeric duplex of any of embodiments 152-157, wherein the conjugate group is attached via the 2' position of a ribosyl sugar moiety at an internal position of the second modified oligonucleotide.

35 Embodiment 161. The oligomeric duplex of any of embodiments 152-160, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

Embodiment 162. The oligomeric duplex of any of embodiments 152-161, wherein the conjugate group comprises a cell-targeting moiety.

Embodiment 163. The oligomeric duplex of any of embodiments 136-162, wherein the second modified oligonucleotide comprises a terminal group.

Embodiment 164. The oligomeric duplex of embodiment 163, wherein the terminal group is an abasic sugar moiety.

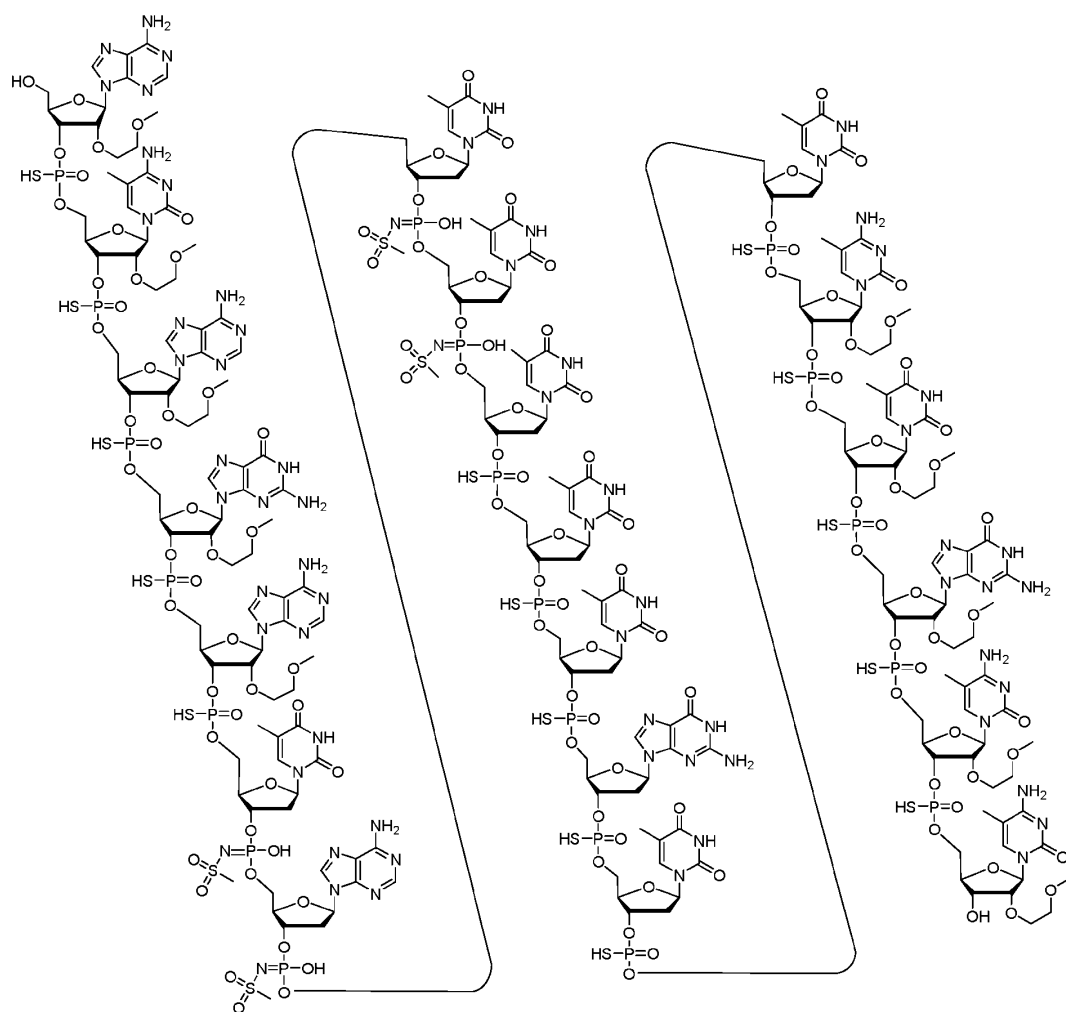
5 Embodiment 165. An antisense agent comprising or consisting of an antisense compound, wherein the antisense compound is the oligomeric compound of any of embodiments 1-135.

Embodiment 166. An antisense agent, wherein the antisense agent is the oligomeric duplex of any of embodiments 136-164.

10 Embodiment 167. The antisense agent of embodiment 165 or embodiment 166, wherein the antisense agent is:
 i) an RNase H agent capable of reducing the amount of SNCA nucleic acid through the activation of RNase H; or
 ii) an RNAi agent capable of reducing the amount of SNCA nucleic acid through the activation of RISC/Ago2.

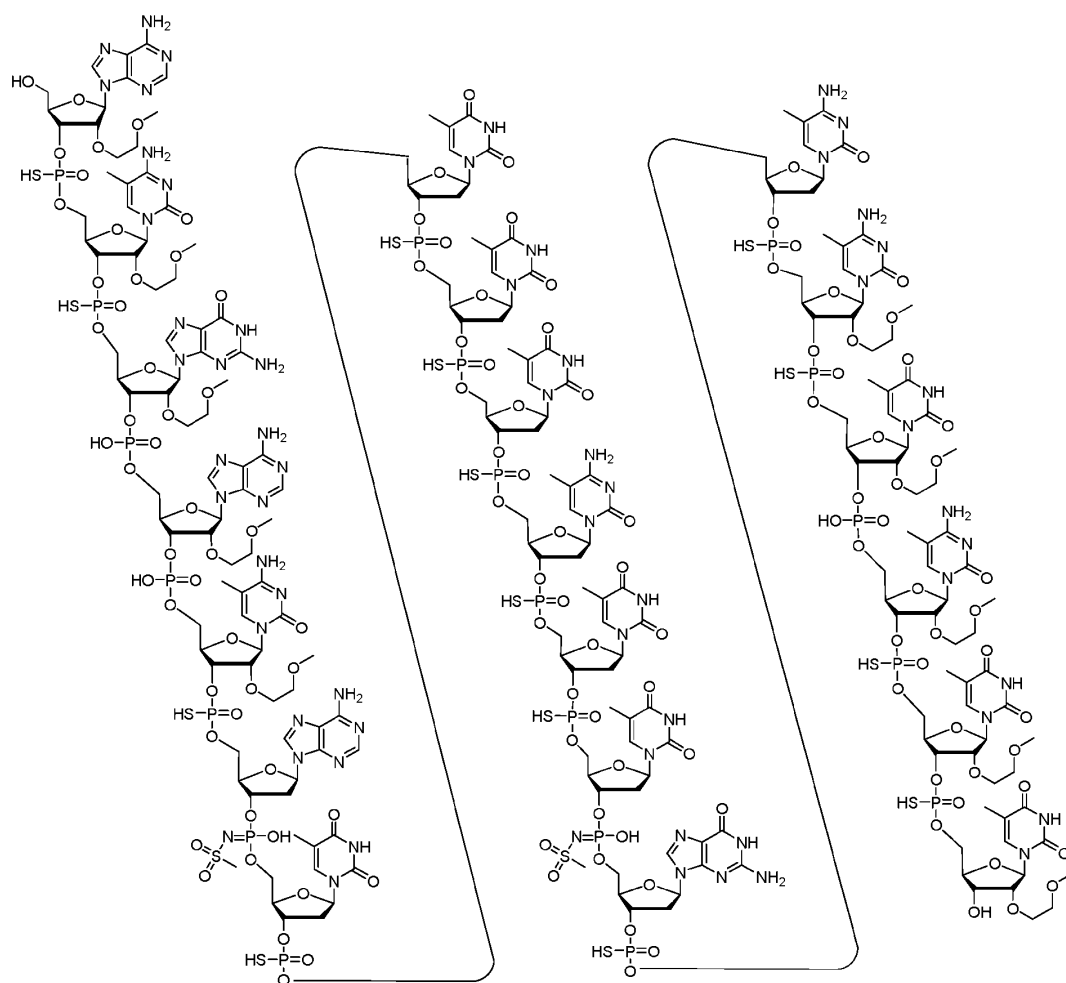
15 Embodiment 168. The antisense agent of any of embodiments 165-167, wherein the antisense agent comprises a conjugate group, and wherein the conjugate group comprises a cell-targeting moiety.

Embodiment 169. A modified oligonucleotide according to the following chemical structure:



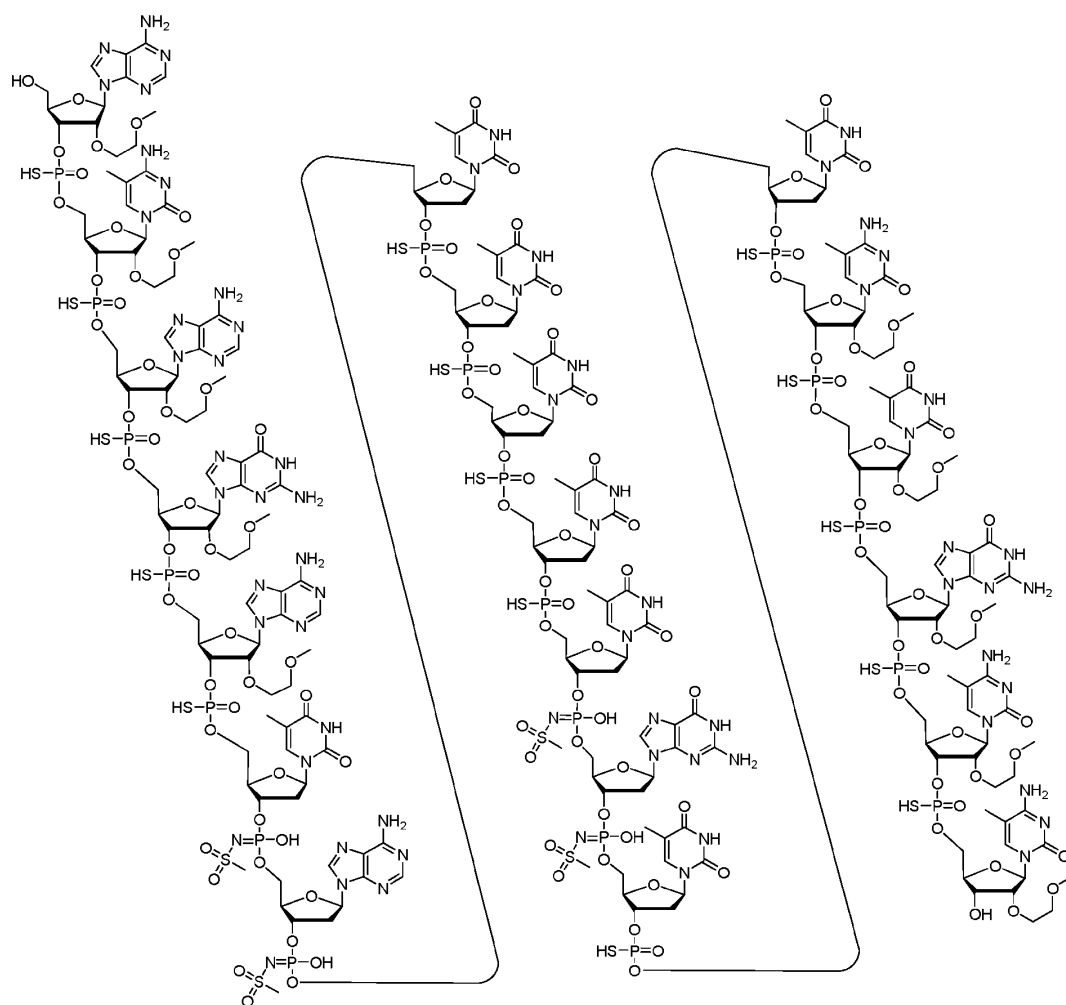
(SEQ ID NO: 3335), or a pharmaceutically acceptable salt thereof.

Embodiment 170. A modified oligonucleotide according to the following chemical structure:



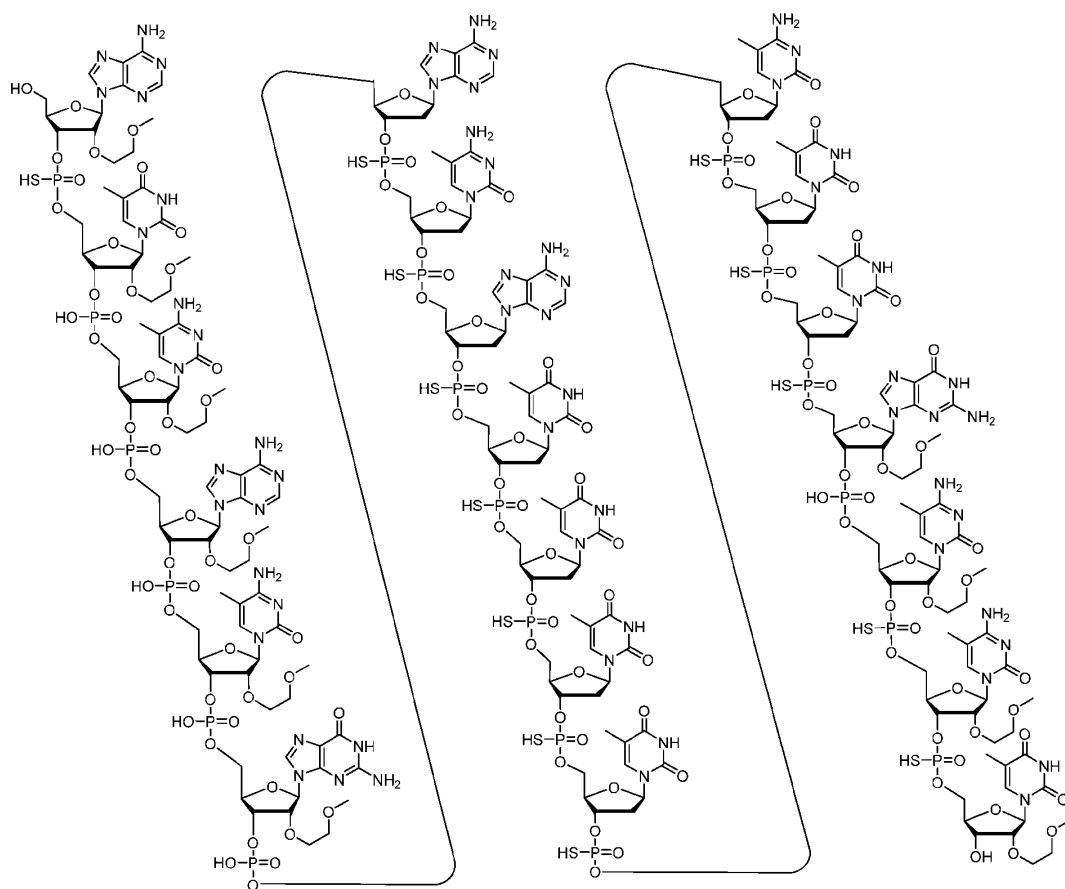
(SEQ ID NO: 3336), or a pharmaceutically acceptable salt thereof.

Embodiment 171. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3337), or a pharmaceutically acceptable salt thereof.

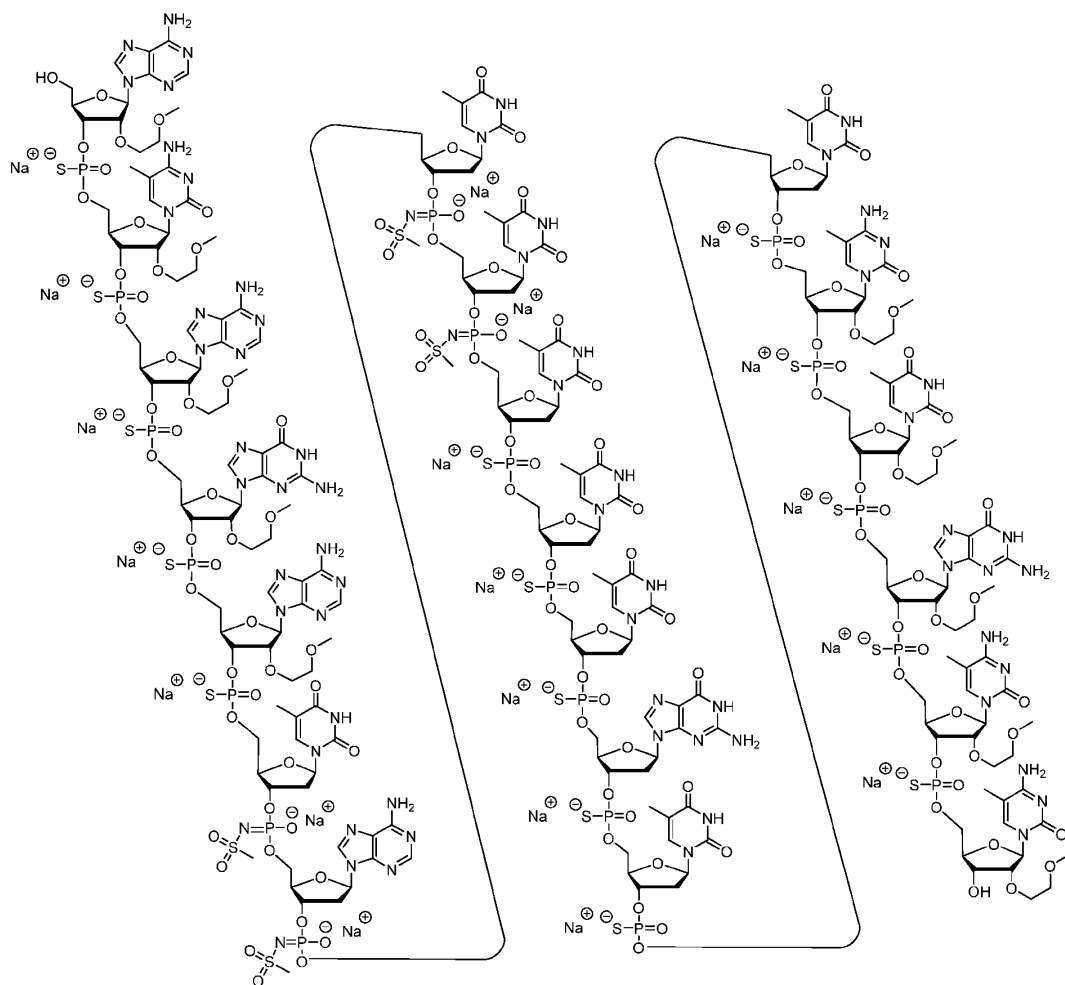
Embodiment 172. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3338), or a pharmaceutically acceptable salt thereof.

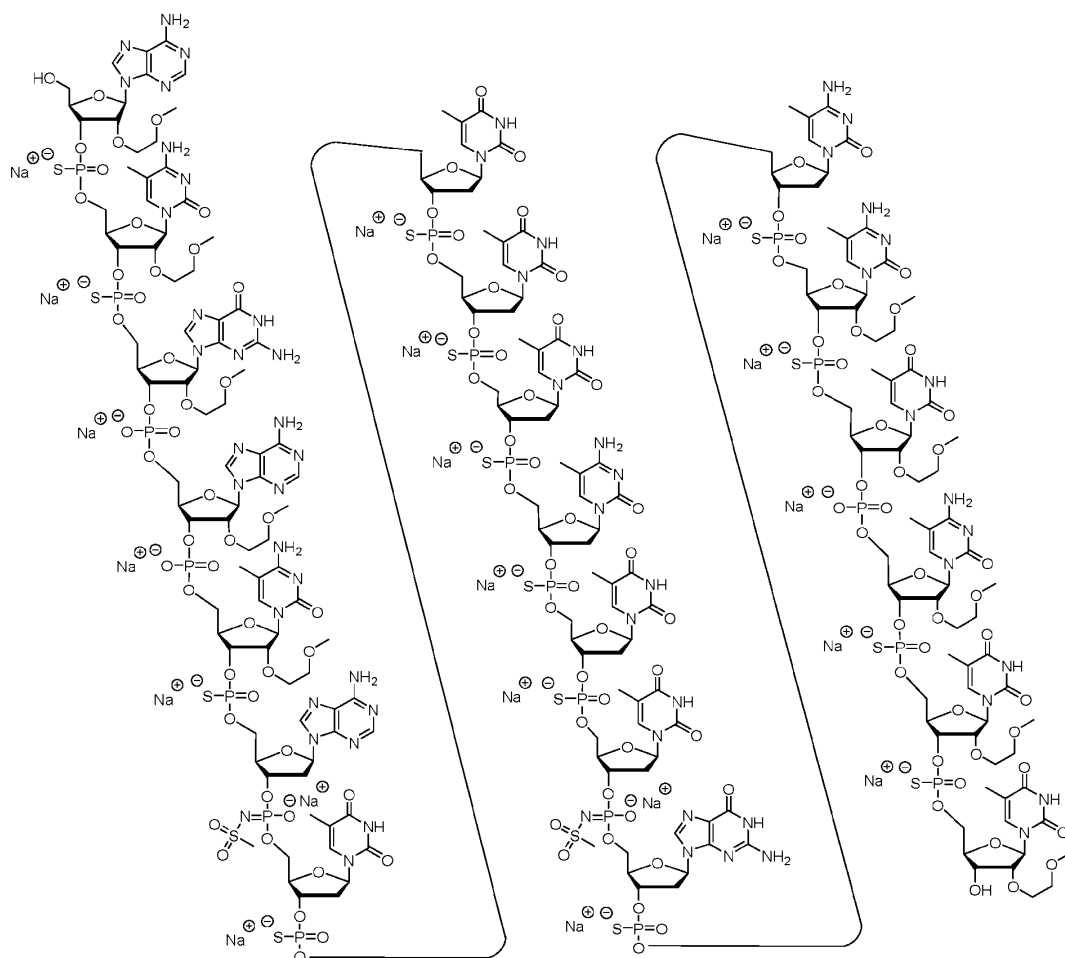
Embodiment 173. The modified oligonucleotide of any of embodiments 169-172, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

Embodiment 174. A modified oligonucleotide according to the following chemical structure:



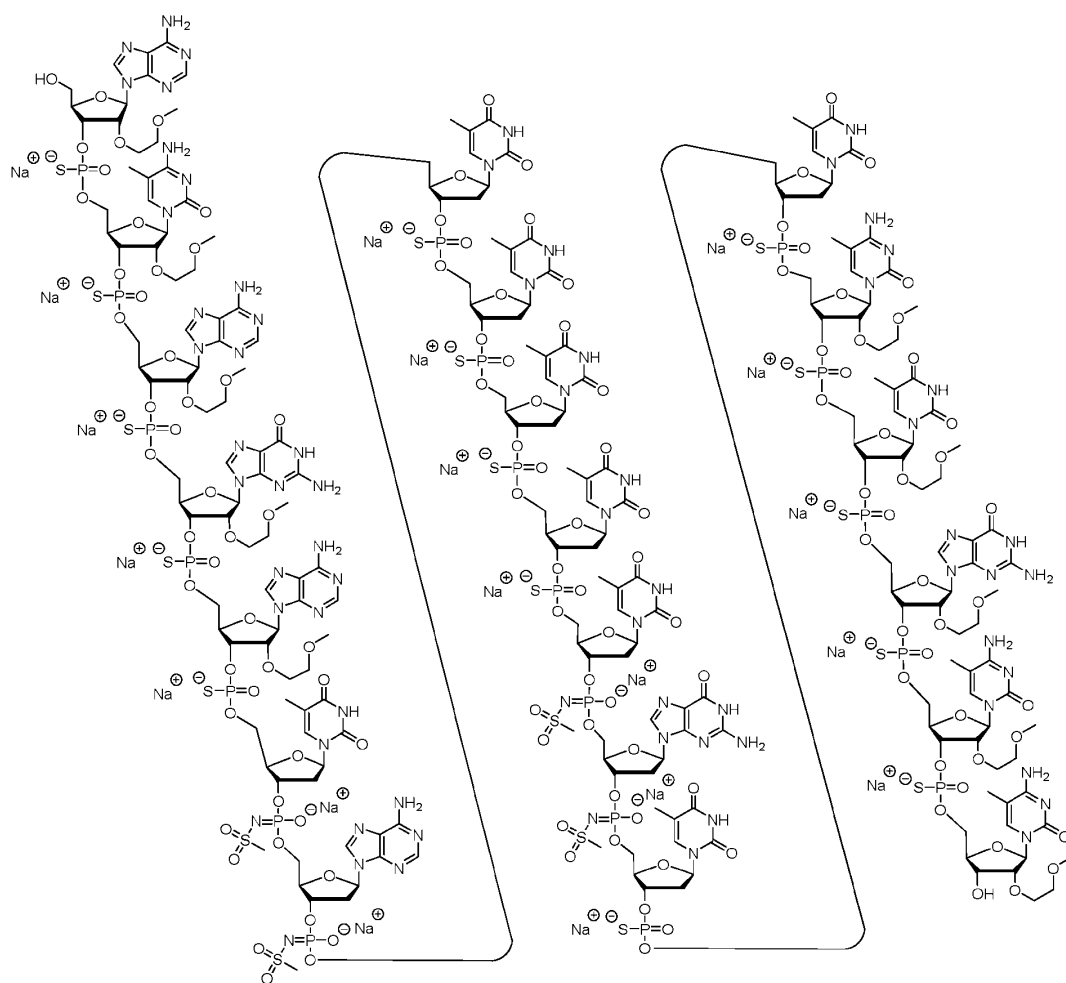
(SEQ ID NO: 3335).

Embodiment 175. A modified oligonucleotide according to the following chemical structure:



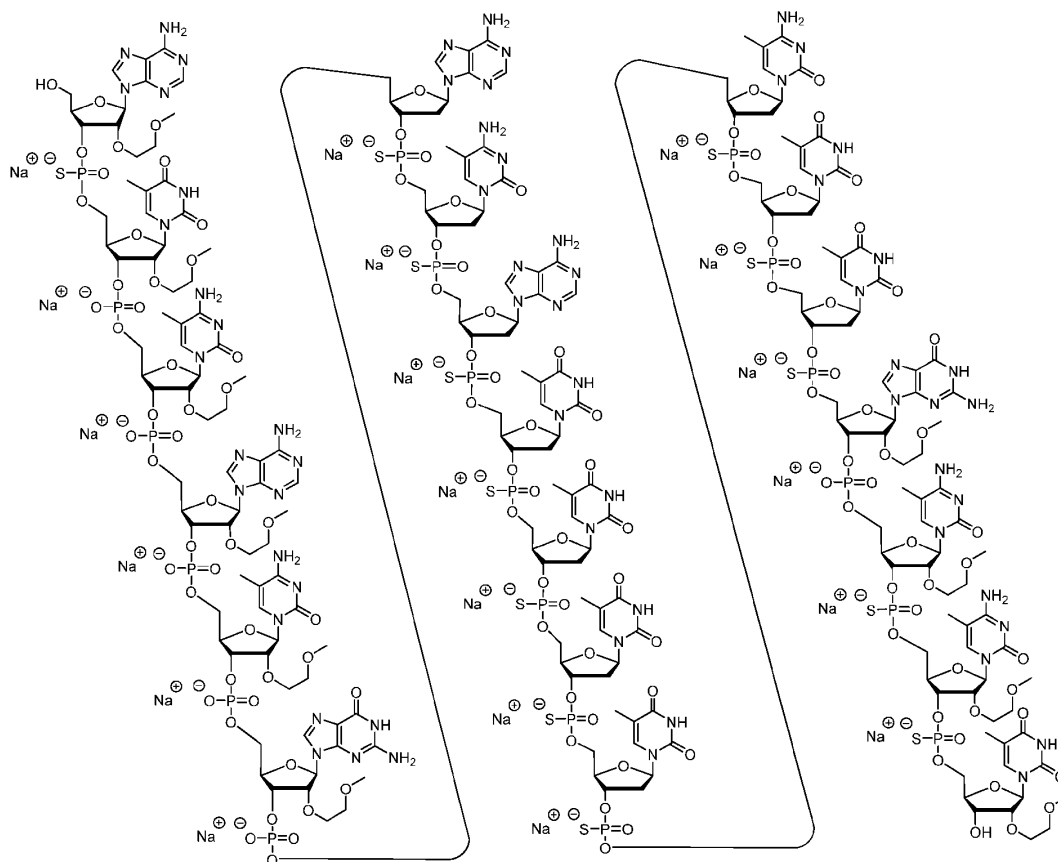
(SEQ ID NO: 3336).

Embodiment 176. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3337).

Embodiment 177. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3338).

Embodiment 178. A population of oligomeric compounds of any of embodiments 1-135 or a population of modified oligonucleotides of any of embodiments 169-177, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

Embodiment 179. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) configuration.

Embodiment 180. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*) configuration.

Embodiment 181. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

Embodiment 182. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides having the (Sp) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (Rp) configuration at each phosphorothioate internucleoside linkage.

Embodiment 183. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides having the (Rp) configuration at one particular phosphorothioate internucleoside linkage and the (Sp) configuration at each of the remaining phosphorothioate internucleoside linkages.

Embodiment 184. The population of embodiment 178, wherein the population is chirally enriched for modified oligonucleotides having at least 3 contiguous phosphorothioate internucleoside linkages in the Sp, Sp, and Rp configurations, in the 5' to 3' direction.

Embodiment 185. A population of oligomeric compounds of any of embodiments 1-135, modified oligonucleotides of any of embodiments 169-177, oligomeric duplexes of any of embodiments 136-164, or antisense agents of any of embodiments 165-168, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

Embodiment 186. A population of oligomeric compounds of any of embodiments 1-135, modified oligonucleotides of any of embodiments 169-177, oligomeric duplexes of any of embodiments 136-164, or antisense agents of any of embodiments 165-168, wherein all of the mesyl phosphoramidate internucleoside linkages of the modified oligonucleotide are stereorandom.

Embodiment 187. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, or a population of any of embodiments 178-186, and a pharmaceutically acceptable diluent.

Embodiment 188. The pharmaceutical composition of embodiment 187, wherein the pharmaceutically acceptable diluent is artificial cerebral spinal fluid (aCSF) or phosphate-buffered saline (PBS).

Embodiment 189. The pharmaceutical composition of embodiment 188, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of embodiments 1-135, the modified oligonucleotide of any of embodiments 169-177, the oligomeric duplex of any of embodiments 136-164, the antisense agent of any of embodiments 165-168, or the population of any of embodiments 178-186, and aCSF.

Embodiment 190. The pharmaceutical composition of embodiment 188, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of embodiments 1-135, the modified oligonucleotide of any of embodiments 169-177, the oligomeric duplex of any of embodiments 136-164, the antisense agent of any of embodiments 165-168, or the population of any of embodiments 178-186, and PBS.

Embodiment 191. A method comprising administering to a subject an oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, a population of any of embodiments 178-186, or a pharmaceutical composition of any of embodiments 187-190.

Embodiment 192. The method of embodiment 191, wherein the subject has or is at risk of developing a synucleinopathy.

Embodiment 193. The method of embodiment 191, wherein the subject has or is at risk of developing Parkinson's disease.

Embodiment 194. The method of embodiment 191, wherein the subject has or is at risk of developing multiple system atrophy (MSA).

Embodiment 195. The method of embodiment 191, wherein the subject has or is at risk of developing dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, neuronopathic Gaucher's disease, or Alzheimer's disease.

Embodiment 196. A method of treating a synucleinopathy comprising administering to a subject having or at risk of developing a synucleinopathy a therapeutically effective amount of an oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, a population of any of embodiments 178-186, or a pharmaceutical composition of any of embodiments 187-190.

Embodiment 197. The method of embodiment 196, wherein the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease.

Embodiment 198. The method of embodiment 196, wherein the synucleinopathy is Parkinson's disease.

Embodiment 199. The method of embodiment 196, wherein the synucleinopathy is multiple system atrophy (MSA).

Embodiment 200. The method of any of embodiments 196-199, wherein at least one symptom or hallmark of synucleinopathy is ameliorated.

Embodiment 201. The method of embodiment 200, wherein the symptom or hallmark is motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.

Embodiment 202. The method of any of embodiments 196-201, wherein administering the oligomeric compound of any of embodiments 1-135, the modified oligonucleotide of any of embodiments 169-177, the oligomeric duplex of any of embodiments 136-164, the antisense agent of any of embodiments 165-168, the population of any of embodiments 178-186, or the pharmaceutical composition of any of embodiments 187-190 reduces or delays the onset or progression of motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.

Embodiment 203. The method of any of embodiments 191-202, wherein the oligomeric compound of any of embodiments 1-135, the modified oligonucleotide of any of embodiments 169-177, the oligomeric duplex of any of embodiments 136-164, the antisense agent of any of embodiments 165-168, the population of any of embodiments 178-186, or the pharmaceutical composition of any of embodiments 187-190 is administered to the central nervous system or systemically.

Embodiment 204. The method of any of embodiments 191-203, wherein the oligomeric compound of any of embodiments 1-135, the modified oligonucleotide of any of embodiments 169-177, the oligomeric duplex of any of embodiments 136-164, the antisense agent of any of embodiments 165-168, the population of any of embodiments 178-186, or the pharmaceutical composition of any of embodiments 187-190 is administered intrathecally.

Embodiment 205. The method of any of embodiments 191-204, wherein the subject is a human.

Embodiment 206. A method of reducing expression of SNCA in a cell comprising contacting the cell with oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an

oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, a population of any of embodiments 178-186, or a pharmaceutical composition of any of embodiments 187-190.

Embodiment 207. The method of embodiment 206, wherein the cell is a brain cell.

Embodiment 208. The method of embodiment 206 or embodiment 207, wherein the cell is a neuron or an oligodendrocyte.

Embodiment 209. The method of any of embodiments 206-208, wherein the cell is a human cell.

Embodiment 210. Use of oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, a population of any of embodiments 178-186, or a pharmaceutical composition of any of embodiments 187-190 for treating a synucleinopathy.

Embodiment 211. Use of oligomeric compound of any of embodiments 1-135, a modified oligonucleotide of any of embodiments 169-177, an oligomeric duplex of any of embodiments 136-164, an antisense agent of any of embodiments 165-168, a population of any of embodiments 178-186, or a pharmaceutical composition of any of embodiments 187-190 for the manufacture of a medicament for treating a synucleinopathy.

Embodiment 212. The use of embodiment 210 or embodiment 211, wherein the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease.

Embodiment 213. The use of embodiment 210 or embodiment 211, wherein the synucleinopathy is Parkinson's disease.

Embodiment 214. The use of embodiment 210 or embodiment 211, wherein the synucleinopathy is multiple system atrophy (MSA).

I. Certain Oligonucleotides

In certain embodiments, provided herein are oligomeric compounds comprising oligonucleotides, which consist of linked nucleosides. Oligonucleotides may be unmodified oligonucleotides (RNA or DNA) or may be modified oligonucleotides. Modified oligonucleotides comprise at least one modification relative to unmodified RNA or DNA. That is, modified oligonucleotides comprise at least one modified nucleoside (comprising a modified sugar moiety and/or a modified nucleobase) and/or at least one modified internucleoside linkage. Certain modified nucleosides and modified internucleoside linkages suitable for use in modified oligonucleotides are described below.

A. Certain Modified Nucleosides

Modified nucleosides comprise a modified sugar moiety or a modified nucleobase or both a modified sugar moiety and a modified nucleobase. In certain embodiments, modified nucleosides comprising the following modified sugar moieties and/or the following modified nucleobases may be incorporated into oligonucleotides.

1. Certain Sugar Moieties

In certain embodiments, modified sugar moieties are non-bicyclic modified sugar moieties. In certain embodiments, modified sugar moieties are bicyclic or tricyclic sugar moieties. In certain embodiments, modified sugar moieties are sugar surrogates. Such sugar surrogates may comprise one or more substitutions corresponding to those of other types of modified sugar moieties.

In certain embodiments, modified sugar moieties are non-bicyclic modified furanosyl sugar moieties comprising one or more acyclic substituent, including, but not limited to, substituents at the 2', 3', 4', and/or 5' positions. In certain embodiments, the furanosyl sugar moiety is a ribosyl sugar moiety. In certain embodiments, one or more acyclic substituent of non-bicyclic modified sugar moieties is branched.

5 In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 2'-position. Examples of substituent groups suitable for the 2'-position of modified sugar moieties include but are not limited to: -F, -OCH₃ ("OMe" or "O-methyl"), and -OCH₂CH₂OCH₃ ("MOE"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF₃, OCF₃, O-C₁-C₁₀ alkoxy, O-C₁-C₁₀ substituted alkoxy, O-C₁-C₁₀ alkyl, O-C₁-C₁₀ substituted alkyl, S-alkyl, N(R_m)-alkyl, O-alkenyl, S-alkenyl, N(R_m)-alkenyl, O-alkynyl, S-alkynyl, N(R_m)-alkynyl, O-alkylenyl-O-alkyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, O(CH₂)₂SCH₃, O(CH₂)₂ON(R_m)(R_n) or OCH₂C(=O)-N(R_m)(R_n), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C₁-C₁₀ alkyl, -O(CH₂)₂ON(CH₃)₂ ("DMAOE"), or 2'-O(CH₂)₂O(CH₂)₂N(CH₃)₂ ("DMAEOE"). And the 2'-substituent groups described in Cook et al., U.S. 6,531,584; Cook et al., U.S. 5,859,221; and Cook et al., U.S. 6,005,087

15 Synthetic methods for some of these 2'-substituent groups can be found in, e.g., Cook et al., U.S. 6,531,584; and Cook et al., U.S. 5,859,221. Certain embodiments of these 2'-substituent groups can be further substituted with one or more substituent groups independently selected from among: hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro (NO₂), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl.

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, NH₂, N₃, OCF₃, OCH₃, O(CH₂)₃NH₂, CH₂CH=CH₂, OCH₂CH=CH₂, OCH₂CH₂OCH₃, O(CH₂)₂SCH₃, O(CH₂)₂ON(R_m)(R_n), O(CH₂)₂O(CH₂)₂N(CH₃)₂, and N-substituted acetamide (OCH₂C(=O)-N(R_m)(R_n)), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C₁-C₁₀ alkyl.

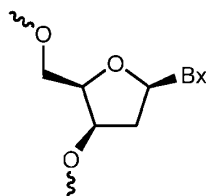
In certain embodiments, a 2'-substituted sugar moiety of a modified nucleoside comprises 2'-substituent group selected from: F, OCF₃, OCH₃, OCH₂CH₂OCH₃, O(CH₂)₂SCH₃, O(CH₂)₂ON(CH₃)₂, O(CH₂)₂O(CH₂)₂N(CH₃)₂, O(CH₂)₂ON(CH₃)₂ ("DMAOE"), O(CH₂)₂O(CH₂)₂N(CH₃)₂ ("DMAEOE"), and OCH₂C(=O)-N(H)CH₃ ("NMA").

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, OCH₃, OCH₂CH₂OCH₃, O(CH₂)₂SCH₃, O(CH₂)₂ON(CH₃)₂, O(CH₂)₂O(CH₂)₂N(CH₃)₂, and OCH₂C(=O)-N(H)CH₃ ("NMA").

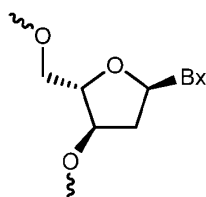
30 In certain embodiments, a 2'-substituted sugar moiety of a modified nucleoside comprises 2'-substituent group selected from: F, OCH₃, and OCH₂CH₂OCH₃.

In certain embodiments, modified furanosyl sugar moieties and nucleosides incorporating such modified furanosyl sugar moieties are further defined by isomeric configuration. For example, a 2'-deoxyfuranosyl sugar moiety may be in seven isomeric configurations other than the naturally occurring β-D-deoxyribose configuration. Such modified sugar moieties are described in, e.g., WO2020/072991. A 2'-modified sugar moiety has an additional stereocenter at the 2'-position relative to a 2'-deoxyfuranosyl sugar moiety; therefore, such sugar moieties have a total of sixteen possible isomeric configurations. Modified furanosyl sugar moieties described herein are in the β-D-ribose isomeric configuration unless otherwise specified.

In certain embodiments, non-bicyclic modified sugar moieties are stereoisomers of DNA, such as 2'-β-D-deoxyxylosyl sugar moiety:



In certain embodiments, a non-bicyclic modified nucleoside comprises a 2'-α-L-deoxyribose sugar moiety:



5

In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 4'-position. Examples of substituent groups suitable for the 4'-position of modified sugar moieties include, but are not limited to, alkoxy (e.g., methoxy), alkyl, and those described in Manoharan et al., WO 2015/106128.

In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 3'-position. Examples of substituent groups suitable for the 3'-position of modified sugar moieties include, but are not limited to, alkoxy (e.g., methoxy), alkyl (e.g., methyl, ethyl).

In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 5'-position. Examples of substituent groups suitable for the 5'-position of modified sugar moieties include, but are not limited to, vinyl, alkoxy (e.g., methoxy), and alkyl (e.g., methyl (*R* or *S*), ethyl).

In certain embodiments, non-bicyclic modified sugar moieties comprise more than one non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties, such as described in Migawa et al., US2010/0190837, or alternative 2'- and 5'-modified sugar moieties as described in Rajeev et al., US2013/0203836.

In naturally occurring nucleic acids, sugars are linked to one another 3' to 5'. In certain embodiments, oligonucleotides include one or more nucleoside or sugar moiety linked at an alternative position, for example at the 2' position or inverted 5' to 3'. For example, where the linkage is at the 2' position, the 2'-substituent groups may instead be at the 3'-position.

Certain modified sugar moieties comprise a substituent that bridges two atoms of the furanosyl ring to form a second ring, resulting in a bicyclic sugar moiety. In certain embodiments, the bicyclic sugar moiety comprises a bridge between the 4' and the 2' furanose ring atoms. Examples of such 4' to 2' bridging sugar substituents include, but are not limited to: 4'-CH₂-2', 4'-(CH₂)₂-2', 4'-(CH₂)₃-2', 4'-CH₂-O-2' ("LNA"), 4'-CH₂-S-2', 4'-(CH₂)₂-O-2' ("ENA"), 4'-CH(CH₃)-O-2' (referred to as "constrained ethyl" or "cEt" when in the *S* configuration), 4'-CH₂-O-CH₂-2', 4'-CH₂-N(R)-2', 4'-CH(CH₂OCH₃)-O-2' ("constrained MOE" or "cMOE") and analogs thereof, 4'-C(CH₃)(CH₃)-O-2' and analogs thereof, 4'-CH₂-N(OCH₃)-2' and analogs thereof, 4'-CH₂-O-N(CH₃)-2', 4'-CH₂-C(H)(CH₃)-2', 4'-CH₂-C(=CH₂)-2' and analogs thereof, 4'-C(R_aR_b)-N(R)-O-2', 4'-C(R_aR_b)-O-N(R)-2', 4'-CH₂-O-N(R)-2', and 4'-CH₂-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C₁-C₁₂ alkyl. Representative U.S. patents

that teach the preparation of such bicyclic sugar moieties include, but are not limited to: Imanishi et al., U.S. 7,427,672; Swayze et al., U.S. 7,741,457, and Swayze et al., U.S. 8,022,193; Seth et al., U.S. 8,278,283; Prakash et al., U.S. 8,278,425; Seth et al., U.S. 8,278,426).

In certain embodiments, such 4' to 2' bridges independently comprise from 1 to 4 linked groups independently selected from: $-\text{C}(\text{R}_a)(\text{R}_b)_n-$, $-\text{C}(\text{R}_a)(\text{R}_b)_n\text{-O-}$, $-\text{C}(\text{R}_a)=\text{C}(\text{R}_b)-$, $-\text{C}(\text{R}_a)=\text{N-}$, $-\text{C}(=\text{NR}_a)-$, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{S})-$, $-\text{O-}$, $-\text{Si}(\text{R}_a)_2-$, $-\text{S}(=\text{O})_x-$, and $-\text{N}(\text{R}_a)-$;

wherein:

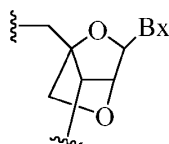
x is 0, 1, or 2;

n is 1, 2, 3, or 4;

each R_a and R_b is, independently, H, a protecting group, hydroxyl, $\text{C}_1\text{-C}_{12}$ alkyl, substituted $\text{C}_1\text{-C}_{12}$ alkyl, $\text{C}_2\text{-C}_{12}$ alkenyl, substituted $\text{C}_2\text{-C}_{12}$ alkenyl, $\text{C}_2\text{-C}_{12}$ alkynyl, substituted $\text{C}_2\text{-C}_{12}$ alkynyl, $\text{C}_5\text{-C}_{20}$ aryl, substituted $\text{C}_5\text{-C}_{20}$ aryl, heterocycle radical, substituted heterocycle radical, heteroaryl, substituted heteroaryl, $\text{C}_5\text{-C}_7$ alicyclic radical, substituted $\text{C}_5\text{-C}_7$ alicyclic radical, halogen, OJ_1 , NJ_1J_2 , SJ_1 , N_3 , COOJ_1 , acyl ($\text{C}(=\text{O})\text{-H}$), substituted acyl, CN, sulfonyl ($\text{S}(=\text{O})_2\text{-J}_1$), or sulfoxyl ($\text{S}(=\text{O})\text{-J}_1$); and each J_1 and J_2 is, independently, H, $\text{C}_1\text{-C}_{12}$ alkyl, substituted $\text{C}_1\text{-C}_{12}$ alkyl, $\text{C}_2\text{-C}_{12}$ alkenyl, substituted $\text{C}_2\text{-C}_{12}$ alkenyl, $\text{C}_2\text{-C}_{12}$ alkynyl, substituted $\text{C}_2\text{-C}_{12}$ alkynyl, $\text{C}_5\text{-C}_{20}$ aryl, substituted $\text{C}_5\text{-C}_{20}$ aryl, acyl ($\text{C}(=\text{O})\text{-H}$), substituted acyl, a heterocycle radical, a substituted heterocycle radical, $\text{C}_1\text{-C}_{12}$ aminoalkyl, substituted $\text{C}_1\text{-C}_{12}$ aminoalkyl, or a protecting group.

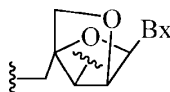
Additional bicyclic sugar moieties are known in the art, see, for example: Wan, *et al.*, *J. Medicinal Chemistry*, 2016, 59, 9645-9667; Wengel *et al.*, U.S. 8,080,644; Ramasamy *et al.*, U.S. 6,525,191; Seth *et al.*, U.S. 7,547,684; and Seth *et al.*, U.S. 7,666,854.

In certain embodiments, bicyclic sugar moieties and nucleosides incorporating such bicyclic sugar moieties are further defined by isomeric configuration. For example, an LNA nucleoside (described herein) may be in the $\alpha\text{-L}$ configuration or in the $\beta\text{-D}$ configuration.



LNA ($\beta\text{-D}$ -configuration)

bridge = $4'\text{-CH}_2\text{-O-}2'$



$\alpha\text{-L}$ -LNA ($\alpha\text{-L}$ -configuration)

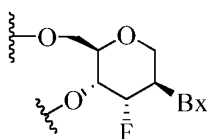
bridge = $4'\text{-CH}_2\text{-O-}2'$

$\alpha\text{-L}$ -methyleneoxy ($4'\text{-CH}_2\text{-O-}2'$) or $\alpha\text{-L}$ -LNA bicyclic nucleosides have been incorporated into oligonucleotides that showed antisense activity (Frieden *et al.*, *Nucleic Acids Research*, 2003, 21, 6365-6372). The addition of locked nucleic acids to siRNAs has been shown to increase siRNA stability in serum, and to reduce off-target effects (Elmen, J. *et al.*, (2005) *Nucleic Acids Research* 33(1):439-447; Mook, OR. *et al.*, (2007) *Mol. Canc. Ther.* 6(3):833-843; Grunweller, A. *et al.*, (2003) *Nucleic Acids Research* 31(12):3185-3193). Herein, general descriptions of bicyclic nucleosides include both isomeric configurations. When the positions of specific bicyclic nucleosides (*e.g.*, LNA or cEt) are identified in exemplified embodiments herein, they are in the $\beta\text{-D}$ configuration, unless otherwise specified.

In certain embodiments, modified sugar moieties comprise one or more non-bridging sugar substituent and one or more bridging sugar substituent (*e.g.*, $5'$ -substituted and $4'\text{-}2'$ bridged sugars).

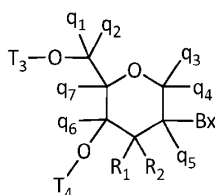
In certain embodiments, modified sugar moieties are sugar surrogates. In certain such embodiments, the oxygen atom of the sugar moiety is replaced, *e.g.*, with a sulfur, carbon or nitrogen atom. In certain such embodiments, such modified sugar moieties also comprise bridging and/or non-bridging substituents as described herein. For example, certain sugar surrogates comprise a 4'-sulfur atom and a substitution at the 2'-position and/or the 5' position.

- 5 In certain embodiments, sugar surrogates comprise rings having other than 5 atoms. For example, in certain embodiments, a sugar surrogate comprises a six-membered tetrahydropyran ("THP"). Such tetrahydropyrans may be further modified or substituted. Nucleosides comprising such modified tetrahydropyrans include, but are not limited to, hexitol nucleic acid ("HNA"), anitol nucleic acid ("ANA"), manitol nucleic acid ("MNA"), fluoro HNA:



F-HNA

- 10 ("F-HNA", *see e.g.*, Egli, et. al., *J Am Chem* (2011) 133(41):16642-16649, Swayze et al., U.S. 8,088,904; and Swayze et al., U.S. 8,440,803) F-HNA can also be referred to as a F-THP or 3'-fluoro tetrahydropyran, and nucleosides comprising additional modified THP compounds having the formula:



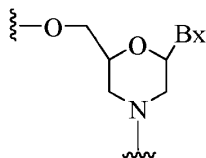
- 15 wherein, independently, for each of said modified THP nucleoside:

Bx is a nucleobase moiety;

- 20 T₃ and T₄ are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T₃ and T₄ is an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T₃ and T₄ is H, a hydroxyl protecting group, a linked conjugate group, or a 5' or 3'-terminal group; q₁, q₂, q₃, q₄, q₅, q₆ and q₇ are each, independently, H, C₁-C₆ alkyl, substituted C₁-C₆ alkyl, C₂-C₆ alkenyl, substituted C₂-C₆ alkenyl, C₂-C₆ alkynyl, or substituted C₂-C₆ alkynyl; and each of R₁ and R₂ is independently selected from among: hydrogen, halogen, substituted or unsubstituted alkoxy, NJ₁J₂, SJ₁, N₃, OC(=X)J₁, OC(=X)NJ₁J₂, NJ₃C(=X)NJ₁J₂, and CN, wherein X is O, S or NJ₁, and each J₁, J₂, and J₃ is, independently, H or C₁-C₆ alkyl.

- 25 In certain embodiments, modified THP nucleosides are provided wherein q₁, q₂, q₃, q₄, q₅, q₆ and q₇ are each H. In certain embodiments, at least one of q₁, q₂, q₃, q₄, q₅, q₆ and q₇ is other than H. In certain embodiments, at least one of q₁, q₂, q₃, q₄, q₅, q₆ and q₇ is methyl. In certain embodiments, modified THP nucleosides are provided wherein one of R₁ and R₂ is F. In certain embodiments, R₁ is F and R₂ is H, in certain embodiments, R₁ is methoxy and R₂ is H, and in certain embodiments, R₁ is methoxyethoxy and R₂ is H.

In certain embodiments, sugar surrogates comprise rings having more than 5 atoms and more than one heteroatom. For example, nucleosides comprising morpholino sugar moieties and their use in oligonucleotides have been reported. As used here, the term “morpholino” means a sugar surrogate having the following structure:



- 5 In certain embodiments, morpholinos may be modified, for example, by adding or altering various substituent groups from the above morpholino structure. Such sugar surrogates are referred to herein as “modified morpholinos.”

In certain embodiments, sugar surrogates comprise acyclic moieties. Examples of nucleosides and oligonucleotides comprising such acyclic sugar surrogates include, but are not limited to: peptide nucleic acid (“PNA”), acyclic butyl nucleic acid), and nucleosides and oligonucleotides described in Manoharan et al., U.S. 10,913,767.

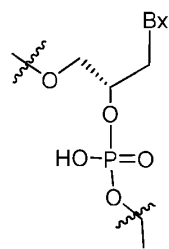
- 10 Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos. 5,539,082; 5,714,331; and 5,719,262.

In certain embodiments, sugar surrogates are the “unlocked” sugar structure of UNA (unlocked nucleic acid) nucleosides. UNA is a nucleoside wherein any of the bonds of the sugar moiety has been removed, forming an unlocked sugar surrogate. A representative U.S. publication that teaches the preparation of UNA includes, but is not limited to, US

- 15 Patent Publication No 2011/0313020.

In certain embodiments, sugar surrogates are the glycerol as found in GNA (glycol nucleic acid) nucleosides as depicted below:

(S)-GNA



- 20

where Bx represents any nucleobase.

Many other bicyclic and tricyclic sugar and sugar surrogates are known in the art that can be used in modified nucleosides.

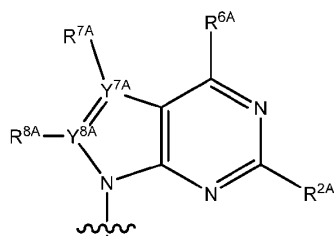
25 2. Certain Modified Nucleobases

In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising an unmodified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising a modified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside that does not comprise a nucleobase, referred to as an abasic nucleoside. In certain embodiments, modified oligonucleotides comprise one or

30 more inosine nucleosides (i.e., nucleosides comprising a hypoxanthine nucleobase). An “unmodified nucleobase” is

adenine (A), thymine (T), cytosine (C), uracil (U), or guanine (G). A modified nucleobase is a group of atoms other than unmodified A, T, C, U, or G capable of pairing with at least one other nucleobase. A 5-methylcytosine is an example of a modified nucleobase. A universal base is a modified nucleobase that can pair with any one of the five unmodified nucleobases.

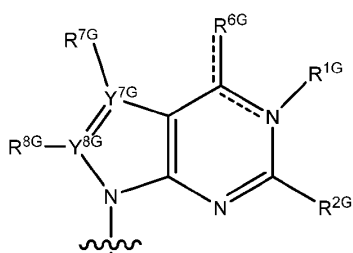
5 In certain embodiments, modified adenine has structure (I):



I

10 wherein: R^{2A} is H, C_1 - C_6 alkyl, substituted C_1 - C_6 alkyl, C_1 - C_6 thioalkyl, or substituted C_1 - C_6 thioalkyl, C_1 - C_6 alkyloxy, or substituted C_1 - C_6 alkyloxy; R^{6A} is H, $N(R^a)(R^b)$, acetyl, formyl, or O-phenyl; Y^{7A} is N and R^{7A} is absent or is C_1 - C_6 alkyl; or Y^{7A} is C and R^{7A} is selected from H, C_1 - C_6 alkyl, or $CN(R^a)(R^b)$; Y^{8A} is N and R^{8A} is absent, or Y^{8A} is C and R^{8A} is selected from H, a halogen, OH, C_1 - C_6 alkyl, or substituted C_1 - C_6 alkyl; R^a and R^b are independently selected from H, C_1 - C_6 alkyl, substituted C_1 - C_6 alkyl, C_1 - C_6 alkenyl, substituted C_1 - C_6 alkenyl, acetyl, formyl, or together form a 5-7-membered heterocycle; excluding where Y^{7A} is N; Y^{8A} is C, R^{8A} is H, R^{2A} is H, and R^{6A} is NH_2 (unmodified adenine).

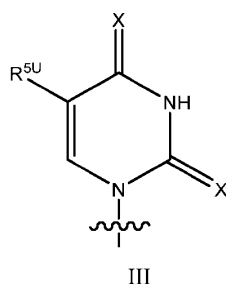
In certain embodiments, modified guanine has structure (II):



II

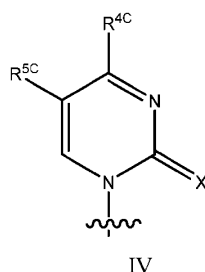
15 wherein: R^{2G} is $N(R^a)(R^b)$; R^{6G} is oxo and R^{1G} is H, or R^{6G} is selected from O- C_1 - C_6 alkyl or S- C_1 - C_6 alkyl and R^{1G} is absent; Y^{7G} is N and R^{7A} is absent or is C_1 - C_6 alkyl; or Y^{7G} is C and R^{7G} is selected from H, C_1 - C_6 alkyl, or $CN(R^a)(R^b)$; Y^{8G} is N and R^{8G} is absent, or Y^{8G} is C and R^{8G} is selected from H, a halogen, OH, C_1 - C_6 alkyl, or substituted C_1 - C_6 alkyl; R^a and R^b are independently selected from H, C_1 - C_6 alkyl, substituted C_1 - C_6 alkyl, C_1 - C_6 alkenyl, substituted C_1 - C_6 alkenyl, acetyl, formyl, or together form a 5-7-membered heterocycle; excluding where Y^{7G} is N; Y^{8G} is C, R^{8G} is H, R^{2G} is NH_2 , and R^{6G} is =O (unmodified guanosine).

In certain embodiments, modified thymine or modified uracil has structure (III):



wherein: X is selected from O or S and R^{5U} is selected from H, OH, halogen, O-C₁-C₁₂ alkyl, O-C₁-C₁₂ substituted alkyl, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₁-C₁₂ alkenyl, substituted C₁-C₁₂ alkenyl; wherein if each X is O, R^{5U} is not H or CH₃ (unmodified uracil and unmodified thymine, respectively).

In certain embodiments, modified cytosine has structure (IV):



wherein: X is selected from O or S, R^{4C} is N(R^a)(R^b); R^{5C} is selected from H, OH, halogen, O-C₁-C₁₂ alkyl, O-C₁-C₁₂ substituted alkyl, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₁-C₁₂ alkenyl, substituted C₁-C₁₂ alkenyl; R^a and R^b are independently selected from H, C₁-C₆ alkyl, substituted C₁-C₆ alkyl, C₁-C₆ alkenyl, substituted C₁-C₆ alkenyl, acetyl, formyl, or together form a 5-7-membered heterocycle; excluding where X is O, R^{4C} is NH₂ and R^{5C} is H (unmodified cytosine).

In certain embodiments, modified nucleobases are 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: 5-methylcytosine, 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≡C-CH₃) 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-isobutylguanidine, 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. Further modified nucleobases include tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one and 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2-one (G-clamp). Modified nucleobases may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Further nucleobases include those disclosed in 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; and those disclosed in Chapters 6 and 15. Antisense Drug Technology, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

Publications that teach the preparation of certain of the above noted modified nucleobases, as well as other modified nucleobases include without limitation, Rogers et al., U.S. 5,134,066 ; Benner et al., U.S. 5,432,272; Matteucci et al., U.S. 5,502,177 ; Froehler et al., U.S. 5,594,121 ; and Cook et al., U.S. 5,681,941.

In certain embodiments, each nucleobase of a modified oligonucleotide of the invention is selected from A, G, C, T, U, and ^mC.

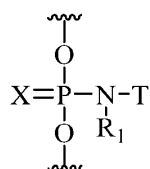
In certain embodiments, each nucleobase of a modified oligonucleotide of the invention is selected from A, G, T, and ^mC (i.e., unmodified purines and 5-methyl pyrimidines).

10

3. Certain Modified Internucleoside Linkages

The naturally occurring internucleoside linkage of RNA and DNA is a 3' to 5' phosphodiester linkage. In certain embodiments, nucleosides of modified oligonucleotides may be linked together using one or more modified internucleoside linkages. The two main classes of internucleoside linking groups are defined by the presence or absence of a phosphorus atom. Representative phosphorus-containing internucleoside linkages include, but are not limited to, phosphodiester, which contain a phosphodiester bond ("P=O") (also referred to as unmodified or naturally occurring linkages), phosphotriesters, methylphosphonates, phosphoramidates, phosphorothioates ("P=S"), and phosphorodithioates ("HS-P=S"). Representative non-phosphorus containing internucleoside linking groups include, but are not limited to, methylenemethylimino (-CH₂-N(CH₃)-O-CH₂-), thiodiester, thionocarbamate (-O-C(=O)(NH)-S-); siloxane (-O-SiH₂-O-); and N,N'-dimethylhydrazine (-CH₂-N(CH₃)-N(CH₃)-). Modified internucleoside linkages, compared to naturally occurring phosphodiester internucleoside linkages, can be used to alter, typically increase, nuclease resistance of the oligonucleotide. In certain embodiments, internucleoside linkages having a chiral atom can be prepared as a racemic mixture, or as separate enantiomers. Methods of preparation of phosphorous-containing and non-phosphorous-containing internucleoside linkages are well known to those skilled in the art.

In certain embodiments, a modified internucleoside linkage is any of those described in WO2021/030778, incorporated by reference herein. In certain embodiments, a modified internucleoside linkage comprises the formula:



wherein independently for each such internucleoside linking group of a modified oligonucleotide:

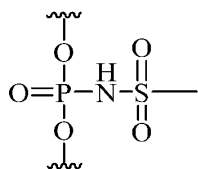
- X is selected from O or S;
- R₁ is selected from H, C₁-C₆ alkyl, and substituted C₁-C₆ alkyl; and
- T is selected from SO₂R₂, C(=O)R₃, and P(=O)R₄R₅, wherein:
 - R₂ is selected from an aryl, a substituted aryl, a heterocycle, a substituted heterocycle, an aromatic heterocycle, a substituted aromatic heterocycle, a diazole, a substituted diazole, a C₁-C₆ alkoxy, C₁-C₆ alkyl, C₁-C₆ alkynyl, C₁-C₆ alkynyl, substituted C₁-C₆ alkyl, substituted C₁-C₆ alkenyl substituted C₁-C₆ alkynyl, and a conjugate group;
 - R₃ is selected from an aryl, a substituted aryl, CH₃, N(CH₃)₂, OCH₃ and a conjugate group;
 - R₄ is selected from OCH₃, OH, C₁-C₆ alkyl, substituted C₁-C₆ alkyl and a conjugate group; and

30

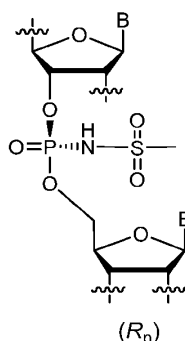
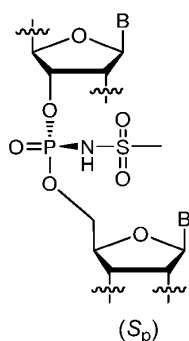
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R₅ is selected from OCH₃, OH, C₁-C₆ alkyl, and substituted C₁-C₆ alkyl.

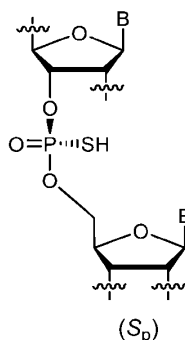
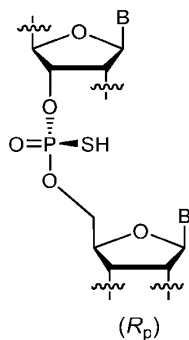
In certain embodiments, a modified internucleoside linkage comprises a mesyl phosphoramidate linking group which has the formula:



- 5 The mesyl phosphoramidate internucleoside linkage comprises a chiral center. In certain embodiments, modified oligonucleotides comprise (*R_p*) and/or (*S_p*) mesyl phosphoramidates, which are shown in the following formulas, respectively, wherein "B" indicates a nucleobase:



- 10 In certain embodiments, a phosphorothioate internucleoside linkage may comprise a chiral center. In certain embodiments, modified oligonucleotides comprising (*R_p*) and/or (*S_p*) phosphorothioates comprise one or more of the following formulas, respectively, wherein "B" indicates a nucleobase:

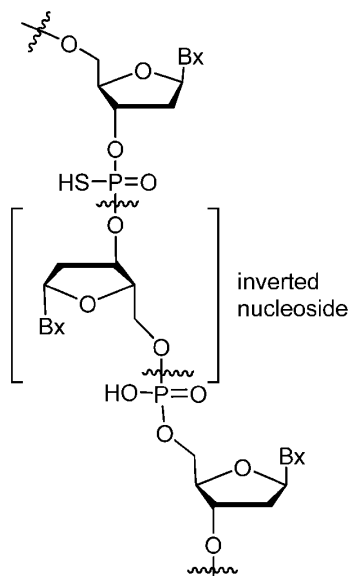


- 15 Representative internucleoside linkages having a chiral center include but are not limited to alkylphosphonates and phosphorothioates. Modified oligonucleotides comprising internucleoside linkages having a chiral center can be prepared as populations of modified oligonucleotides comprising stereorandom internucleoside linkages, or as populations of modified oligonucleotides comprising such internucleoside linkages in particular stereochemical configurations. In certain embodiments, populations of modified oligonucleotides comprise phosphorothioate internucleoside linkages wherein all of the phosphorothioate internucleoside linkages are stereorandom. In certain

embodiments, populations of modified oligonucleotides comprise mesyl phosphoramidate internucleoside linkages wherein all of the mesyl phosphoramidate internucleoside linkages are stereorandom. Such modified oligonucleotides can be generated using synthetic methods that result in random selection of the stereochemical configuration of each internucleoside linkage having a chiral center. Nonetheless, each individual internucleoside linkage having a chiral center of each individual oligonucleotide molecule has a defined stereoconfiguration. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising one or more particular phosphorothioate and/or mesyl phosphoramidate internucleoside linkages, each independently in a particular, independently selected stereochemical configuration. In certain embodiments, the particular configuration of the particular phosphorothioate and/or mesyl phosphoramidate linkage is present in at least 65% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate and/or mesyl phosphoramidate linkage is present in at least 70% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate and/or mesyl phosphoramidate linkage is present in at least 80% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate and/or mesyl phosphoramidate linkage is present in at least 90% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate and/or mesyl phosphoramidate linkage is present in at least 99% of the molecules in the population. Such chirally enriched populations of modified oligonucleotides can be generated using synthetic methods known in the art, *e.g.*, methods described in Oka et al., *JACS* 125, 8307 (2003), Wan et al. *Nucleic Acids Res.* 42, 13456 (2014), and WO 2017/015555. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one indicated phosphorothioate and/or mesyl phosphoramidate in the (Sp) configuration. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one phosphorothioate and/or mesyl phosphoramidate in the (Rp) configuration. Unless otherwise indicated, internucleoside linkages having chiral centers of modified oligonucleotides described herein can be stereorandom or in a particular stereochemical configuration.

Neutral internucleoside linkages include, without limitation, phosphotriesters, methylphosphonates, MMI (3'-CH₂-N(CH₃)-O-5'), amide-3 (3'-CH₂-C(=O)-N(H)-5'), amide-4 (3'-CH₂-N(H)-C(=O)-5'), formacetal (3'-O-CH₂-O-5'), methoxypropyl (MOP), and thioformacetal (3'-S-CH₂-O-5'). Further neutral internucleoside linkages include nonionic linkages comprising siloxane (dialkylsiloxane), carboxylate ester, carboxamide, sulfide, sulfonate ester and amides (See for example: *Carbohydrate Modifications in Antisense Research*; Y.S. Sanghvi and P.D. Cook, Eds., ACS Symposium Series 580; Chapters 3 and 4, 40-65). Further neutral internucleoside linkages include nonionic linkages comprising mixed N, O, S and CH₂ component parts.

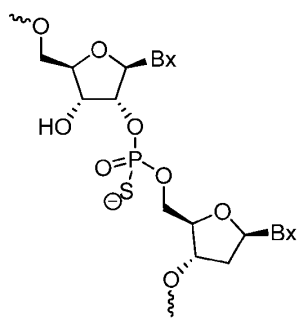
In certain embodiments, modified oligonucleotides comprise one or more inverted nucleoside, as shown below:



wherein each Bx independently represents any nucleobase.

- 5 In certain embodiments, an inverted nucleoside is terminal (i.e., the last nucleoside on one end of an oligonucleotide) and so only one internucleoside linkage depicted above will be present. In certain such embodiments, additional features (such as a conjugate group) may be attached to the inverted nucleoside. Such terminal inverted nucleosides can be attached to either or both ends of an oligonucleotide.

- 10 In certain embodiments, nucleic acids can be linked 2' to 5' rather than the standard 3' to 5' linkage. Such a linkage is illustrated below.



wherein each Bx represents any nucleobase.

15 B. Certain Motifs

In certain embodiments, modified oligonucleotides comprise one or more modified nucleosides comprising a modified sugar moiety. In certain embodiments, modified oligonucleotides comprise one or more modified nucleosides comprising a modified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more modified

internucleoside linkage. In such embodiments, the modified, unmodified, and differently modified sugar moieties, nucleobases, and/or internucleoside linkages of a modified oligonucleotide define a pattern or motif. In certain embodiments, the patterns of sugar moieties, nucleobases, and internucleoside linkages are each independent of one another. Thus, a modified oligonucleotide may be described by its sugar motif, nucleobase motif and/or internucleoside linkage motif (as used herein, nucleobase motif describes the modifications to the nucleobases independent of the sequence of nucleobases).

1. Certain Sugar Motifs

In certain embodiments, oligonucleotides comprise one or more type of modified sugar and/or unmodified sugar moiety arranged along the oligonucleotide or region thereof in a defined pattern or sugar motif. In certain instances, such sugar motifs include but are not limited to any of the sugar modifications discussed herein.

In certain embodiments, modified oligonucleotides comprise a deoxy region. In certain embodiments, each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside. In certain embodiments, the deoxy region consists of 5-12 linked nucleosides. In certain embodiments, the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides. In certain embodiments, at least one nucleoside within the deoxy region comprises a modified sugar moiety. In certain embodiments, exactly one nucleoside within the deoxy region comprises a modified sugar moiety. In certain embodiments, two or three nucleosides within the deoxy region comprise a modified sugar moiety.

In certain embodiments, the deoxy region is flanked on the 5'-side by a 5'-region consisting of linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of linked 3'-region nucleosides; wherein the 3'-most nucleoside of the 5'-region is a modified nucleoside and the 5'-most nucleoside of the 3'-region is a modified nucleoside. At least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety. The three regions (the 5'-region, the deoxy region, and the 3'-region) form a contiguous sequence of nucleosides. In certain embodiments, the sugar moiety of the 3'-most nucleoside of the 5'-region and the sugar moiety of the 5'-most nucleoside of the 3'-region each differ from the sugar moiety of the respective adjacent nucleoside of the deoxy region, thus defining the boundary between the 5'-region, the deoxy region, and the 3'-region. In certain embodiments, each nucleoside of the 5'-region and each nucleoside of the 3'-region comprises a modified sugar moiety. In certain embodiments, the nucleosides within the 5'-region comprise the same sugar modification. In certain embodiments, the nucleosides within the 5'-region comprise two or more different sugar modifications. In certain embodiments, the nucleosides within the 3'-region comprise the same sugar modification. In certain embodiments, the nucleosides within the 3'-region comprise two or more different sugar modifications.

In certain embodiments, the 5'-region and the 3'-region of a modified oligonucleotide each comprises 1-8 nucleosides. In certain embodiments, the 5'-region comprises 1-7 nucleosides. In certain embodiments, the 5'-region comprises 1-6 nucleosides. In certain embodiments, the 5'-region comprises 1, 2, 3, 4, 5, 6, 7, or 8 nucleosides. In certain embodiments, the 3'-region comprises 1-7 nucleosides. In certain embodiments, the 3'-region comprises 1-6 nucleosides. In certain embodiments, the 3'-region comprises 1, 2, 3, 4, 5, 6, 7, or 8 nucleosides.

In certain embodiments, modified oligonucleotides comprise or consist of a region having a gapmer motif, which is defined by two external regions or "wings" and a central or internal region or "gap." The three regions of a gapmer motif (the 5'-wing, the gap, and the 3'-wing) form a contiguous sequence of nucleosides wherein at least some of the sugar moieties of the nucleosides of each of the wings differ from at least some of the sugar moieties of the

nucleosides of the gap. Specifically, at least the sugar moieties of the nucleosides of each wing that are closest to the gap (the 3'-most nucleoside of the 5'-wing and the 5'-most nucleoside of the 3'-wing) differ from the sugar moiety of the neighboring gap nucleosides, thus defining the boundary between the wings and the gap (i.e., the wing/gap junction). In certain embodiments, the sugar moieties within the gap are the same as one another. In certain embodiments, the gap includes one or more nucleoside having a sugar moiety that differs from the sugar moiety of one or more other nucleosides of the gap. In certain embodiments, the sugar motifs of the two wings are the same as one another (symmetric gapmer). In certain embodiments, the sugar motif of the 5'-wing differs from the sugar motif of the 3'-wing (asymmetric gapmer).

In certain embodiments, the wings of a gapmer comprise 1-6 nucleosides. In certain embodiments, each nucleoside of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least one nucleoside of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least two nucleosides of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least three nucleosides of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least four nucleosides of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least five nucleosides of each wing of a gapmer comprises a modified sugar moiety.

In certain embodiments, the gap of a gapmer comprises 7-12 nucleosides. In certain embodiments, each nucleoside of the gap of a gapmer comprises a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, at least one nucleoside of the gap of a gapmer comprises a modified sugar moiety.

In certain embodiments, the gapmer is a deoxy gapmer. In certain embodiments, the nucleosides on the gap side of each wing/gap junction comprise 2'-β-D-deoxyribose sugar moieties and the nucleosides on the wing sides of each wing/gap junction comprise modified sugar moieties. In certain embodiments, each nucleoside of the gap comprises a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, each nucleoside of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, at least one nucleoside of the gap of a gapmer comprises a modified sugar moiety. In certain embodiments, at least one nucleoside of the gap of a gapmer comprises a 2'-OMe sugar moiety.

In certain embodiments, modified oligonucleotides comprise or consist of a portion having a fully modified sugar motif. In such embodiments, each nucleoside of the fully modified portion of the modified oligonucleotide comprises a modified sugar moiety. In certain embodiments, each nucleoside of the entire modified oligonucleotide comprises a modified sugar moiety. In certain embodiments, modified oligonucleotides comprise or consist of a portion having a fully modified sugar motif, wherein each nucleoside within the fully modified portion comprises the same modified sugar moiety, referred to herein as a uniformly modified sugar motif. In certain embodiments, a fully modified oligonucleotide is a uniformly modified oligonucleotide. In certain embodiments, each nucleoside of a uniformly modified oligonucleotide comprises the same 2'-modification.

Herein, the lengths (number of nucleosides) of the three regions of a gapmer may be provided using the notation [# of nucleosides in the 5'-wing] – [# of nucleosides in the gap] – [# of nucleosides in the 3'-wing]. Thus, a 3-10-3 gapmer consists of 3 linked nucleosides in each wing and 10 linked nucleosides in the gap. Where such nomenclature is followed by a specific modification, that modification is the modification in each sugar moiety of each wing and the gap nucleosides comprise 2'-β-D-deoxyribose sugar moieties. Thus, a 5-10-5 MOE gapmer consists of 5 linked 2'-MOE nucleosides in the 5'-wing, 10 linked 2'-β-D-deoxynucleosides in the gap, and 5 linked 2'-MOE nucleosides in the 3'-wing. A 3-10-3 cEt gapmer consists of 3 linked cEt nucleosides in the 5'-wing, 10 linked 2'-β-D-

deoxynucleosides in the gap, and 3 linked cEt nucleosides in the 3'-wing. A 5-8-5 gapmer consists of 5 linked nucleosides comprising a modified sugar moiety in the 5'-wing, 8 linked 2'-β-D-deoxynucleosides in the gap, and 5 linked nucleosides comprising a modified sugar moiety in the 3'-wing. A 5-8-5 mixed gapmer has at least two different modified sugar moieties in the 5'- and/or the 3'-wing, two different modified sugar moieties in the gap region, or a combination thereof.

In certain embodiments, modified oligonucleotides disclosed herein are modified by a specific sugar modification. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 BNA gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 cEt gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 LNA gapmers. In certain embodiments, modified oligonucleotides are 3-10-4 cEt gapmers. In certain embodiments, modified oligonucleotides are 4-10-3 cEt gapmers. In certain embodiments, modified oligonucleotides are 4-10-4 cEt gapmers. In certain embodiments, 5-10-5 cEt gapmers. In certain embodiments, modified oligonucleotides are 6-10-4 MOE gapmers.

In certain embodiments, modified oligonucleotides disclosed herein are modified by two or more sugar modifications. In certain embodiments, modified oligonucleotides are 3-10-3 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties. In certain embodiments, modified oligonucleotides are 3-10-4 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties. In certain embodiments, modified oligonucleotides are 3-10-5 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties. In certain embodiments, modified oligonucleotides are 4-9-4 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties. In certain embodiments, modified oligonucleotides are 5-10-5 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties. In certain embodiments, modified oligonucleotides are 6-10-4 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a modified sugar moiety selected from a 2'-MOE sugar moiety and a 2'-cEt sugar moiety, and the gap nucleosides comprise 2'-β-D-deoxyribsyl sugar moieties.

In certain embodiments, modified oligonucleotides disclosed herein are modified by two or more sugar modifications within the gap region. In certain embodiments, modified oligonucleotides are 3-10-3 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a 2'-cEt sugar moiety, and each nucleoside within the gap comprises a sugar moiety selected from a 2'-OMe sugar moiety or a 2'-β-D-deoxyribsyl sugar moiety. In certain embodiments, modified oligonucleotides are 5-10-5 mixed gapmers, wherein each nucleoside within the 5' and the 3' wings comprises a 2'-MOE sugar moiety, and each nucleoside within the gap comprises a sugar moiety selected from a 2'-β-D-deoxyxylosyl sugar moiety, a 2'-α-L-deoxyribsyl sugar moiety, and 2'-β-D-deoxyribsyl sugar moiety.

[illegible]

kkkddddddeee -3', 5'- ekkddddddeee -3', 5'- kkkddddddeee -3', 5'- eeeedddddeee -3',
 5'- eeeedddddeee -3', 5'- eeeedddddeee -3', 5'- eeeed[bDdx]ddddeee -3', 5'-
 eeeedd[bDdx]ddddeee -3', 5'- eeeed[aLdr]ddddeee -3', 5'- eeeedd[aLdr]ddddeee -3', and 5'-
 eekddddddeee -3', wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, each "e" represents a 2'-
 5 MOE sugar moiety, each "k" represents a cEt sugar moiety, each "y" represents a 2'-O-methyl sugar moiety, each
 "[bDdx]" represents a 2'-β-D-deoxyxylosyl sugar moiety, and each "[aLdr]" represents a 2'-α-L-deoxyribose sugar
 moiety. In certain embodiments, modified oligonucleotides have a sugar motif of 5'- eeeedddddeee -3',
 wherein each "e" represents a 2'-MOE sugar moiety, and each "d" represents a 2'-β-D-deoxyribose sugar moiety. In
 certain embodiments, modified oligonucleotides have a sugar motif of 5'- eeeedddddeee -3', wherein each "e"
 10 represents a 2'-MOE sugar moiety, and each "d" represents a 2'-β-D-deoxyribose sugar moiety.

2. Certain Nucleobase Motifs

In certain embodiments, oligonucleotides comprise modified and/or unmodified nucleobases arranged along the
 oligonucleotide or region thereof in a defined pattern or motif. In certain embodiments, each nucleobase is modified. In
 15 certain embodiments, none of the nucleobases are modified. In certain embodiments, each purine or each pyrimidine is
 modified. In certain embodiments, each adenine is modified. In certain embodiments, each guanine is modified. In
 certain embodiments, each thymine is modified. In certain embodiments, each uracil is modified. In certain
 embodiments, each cytosine is modified. In certain embodiments, some or all of the cytosine nucleobases in a modified
 oligonucleotide are 5-methylcytosines. In certain embodiments, all of the cytosine nucleobases are 5-methylcytosines
 20 and all of the other nucleobases of the modified oligonucleotide are unmodified nucleobases.

In certain embodiments, modified oligonucleotides comprise a block of modified nucleobases. In certain such
 embodiments, the block is at the 3'-end of the oligonucleotide. In certain embodiments the block is within 3 nucleosides
 of the 3'-end of the oligonucleotide. In certain embodiments, the block is at the 5'-end of the oligonucleotide. In certain
 embodiments the block is within 3 nucleosides of the 5'-end of the oligonucleotide.

In certain embodiments, oligonucleotides having a gapmer motif comprise a nucleoside comprising a modified
 nucleobase. In certain such embodiments, one nucleoside comprising a modified nucleobase is in the central gap of an
 oligonucleotide having a gapmer motif. In certain such embodiments, the sugar moiety of said nucleoside is a 2'- β-D-
 deoxyribose sugar moiety. In certain embodiments, the modified nucleobase is selected from a 2-thiopyrimidine and a
 5-propynepyrimidine.

30

3. Certain Internucleoside Linkage Motifs

In certain embodiments, oligonucleotides comprise modified and/or unmodified internucleoside linkages
 arranged along the oligonucleotide or region thereof in a defined pattern or motif. In certain embodiments, each
 internucleoside linking group is a phosphodiester internucleoside linkage (P=O). In certain embodiments, each
 35 internucleoside linking group of a modified oligonucleotide is a phosphorothioate internucleoside linkage (P=S). In
 certain embodiments, each internucleoside linkage of a modified oligonucleotide is independently selected from a
 phosphorothioate internucleoside linkage and phosphodiester internucleoside linkage. In certain embodiments, each
 phosphorothioate internucleoside linkage is independently selected from a stereorandom phosphorothioate (Sp)
 phosphorothioate, and a (Rp) phosphorothioate.

In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer and the internucleoside linkages within the gap are all modified. In certain embodiments, some or all of the internucleoside linkages in the wings are unmodified phosphodiester internucleoside linkages. In certain embodiments, the terminal internucleoside linkages are modified. In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer, and the internucleoside linkage motif comprises at least one phosphodiester internucleoside linkage in at least one wing, wherein the at least one phosphodiester linkage is not a terminal internucleoside linkage, and the remaining internucleoside linkages are phosphorothioate internucleoside linkages. In certain such embodiments, all of the phosphorothioate linkages are stereorandom. In certain embodiments, all of the phosphorothioate linkages in the wings are (Sp) phosphorothioates, and the gap comprises at least one Sp, Sp, or Rp motif. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising such internucleoside linkage motifs.

In certain embodiments, modified oligonucleotides have an internucleoside linkage motif comprising one or more mesyl phosphoramidate linking groups. In certain embodiments, one or more phosphorothioate internucleoside linkages or one or more phosphodiester internucleoside linkages of the internucleoside linkage motifs herein is substituted with a mesyl phosphoramidate linking group.

[illegible]

oligonucleotides have an internucleoside linkage motif of 5'-sooooooooooooo-3', wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

C. Certain Lengths

5 It is possible to increase or decrease the length of an oligonucleotide without eliminating activity. For example, in Woolf et al. (Proc. Natl. Acad. Sci. USA 89:7305-7309, 1992), a series of oligonucleotides 13-25 nucleobases in length were tested for their ability to induce cleavage of a target RNA in an oocyte injection model. Oligonucleotides 25 nucleobases in length with 8 or 11 mismatch bases near the ends of the oligonucleotides were able to direct specific cleavage of the target RNA, albeit to a lesser extent than the oligonucleotides that contained no mismatches. Similarly, target specific cleavage was achieved using 13 nucleobase oligonucleotides, including those with 1 or 3 mismatches.

In certain embodiments, oligonucleotides (including modified oligonucleotides) can have any of a variety of ranges of lengths. In certain embodiments, oligonucleotides consist of X to Y linked nucleosides, where X represents the fewest number of nucleosides in the range and Y represents the largest number nucleosides in the range. In certain such embodiments, X and Y are each independently selected from 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, and 50; provided that $X \leq Y$. For example, in certain embodiments, oligonucleotides consist of 12 to 13, 12 to 14, 12 to 15, 12 to 16, 12 to 17, 12 to 18, 12 to 19, 12 to 20, 12 to 21, 12 to 22, 12 to 23, 12 to 24, 12 to 25, 12 to 26, 12 to 27, 12 to 28, 12 to 29, 12 to 30, 13 to 14, 13 to 15, 13 to 16, 13 to 17, 13 to 18, 13 to 19, 13 to 20, 13 to 21, 13 to 22, 13 to 23, 13 to 24, 13 to 25, 13 to 26, 13 to 27, 13 to 28, 13 to 29, 13 to 30, 14 to 15, 14 to 16, 14 to 17, 14 to 18, 14 to 19, 14 to 20, 14 to 21, 14 to 22, 14 to 23, 14 to 24, 14 to 25, 14 to 26, 14 to 27, 14 to 28, 14 to 29, 14 to 30, 15 to 16, 15 to 17, 15 to 18, 15 to 19, 15 to 20, 15 to 21, 15 to 22, 15 to 23, 15 to 24, 15 to 25, 15 to 26, 15 to 27, 15 to 28, 15 to 29, 15 to 30, 16 to 17, 16 to 18, 16 to 19, 16 to 20, 16 to 21, 16 to 22, 16 to 23, 16 to 24, 16 to 25, 16 to 26, 16 to 27, 16 to 28, 16 to 29, 16 to 30, 17 to 18, 17 to 19, 17 to 20, 17 to 21, 17 to 22, 17 to 23, 17 to 24, 17 to 25, 17 to 26, 17 to 27, 17 to 28, 17 to 29, 17 to 30, 18 to 19, 18 to 20, 18 to 21, 18 to 22, 18 to 23, 18 to 24, 18 to 25, 18 to 26, 18 to 27, 18 to 28, 18 to 29, 18 to 30, 19 to 20, 19 to 21, 19 to 22, 19 to 23, 19 to 24, 19 to 25, 19 to 26, 19 to 27, 19 to 28, 19 to 29, 19 to 30, 20 to 21, 20 to 22, 20 to 23, 20 to 24, 20 to 25, 20 to 26, 20 to 27, 20 to 28, 20 to 29, 20 to 30, 21 to 22, 21 to 23, 21 to 24, 21 to 25, 21 to 26, 21 to 27, 21 to 28, 21 to 29, 21 to 30, 22 to 23, 22 to 24, 22 to 25, 22 to 26, 22 to 27, 22 to 28, 22 to 29, 22 to 30, 23 to 24, 23 to 25, 23 to 26, 23 to 27, 23 to 28, 23 to 29, 23 to 30, 24 to 25, 24 to 26, 24 to 27, 24 to 28, 24 to 29, 24 to 30, 25 to 26, 25 to 27, 25 to 28, 25 to 29, 25 to 30, 26 to 27, 26 to 28, 26 to 29, 26 to 30, 27 to 28, 27 to 29, 27 to 30, 28 to 29, 28 to 30, or 29 to 30 linked nucleosides.

In certain embodiments, oligonucleotides (including modified oligonucleotides) consist of 16 linked nucleosides. In certain embodiments, oligonucleotides (including modified oligonucleotides) consist of 17 linked nucleosides. In certain embodiments, oligonucleotides (including modified oligonucleotides) consist of 18 linked nucleosides. In certain embodiments, oligonucleotides (including modified oligonucleotides) consist of 19 linked nucleosides. In certain embodiments, oligonucleotides (including modified oligonucleotides) consist of 20 linked nucleosides.

D. Certain Modified Oligonucleotides

In certain embodiments, the above modifications (sugar, nucleobase, internucleoside linkage) are incorporated into a modified oligonucleotide. In certain embodiments, modified oligonucleotides are characterized by their

modification motifs and overall lengths. In certain embodiments, such parameters are each independent of one another. Thus, unless otherwise indicated, each internucleoside linkage of an oligonucleotide having a gapmer sugar motif may be modified or unmodified and may or may not follow the gapmer modification pattern of the sugar modifications. For example, the internucleoside linkages within the wing regions of a sugar gapmer may be the same or different from one another and may be the same or different from the internucleoside linkages of the gap region of the sugar motif. Likewise, such sugar gapmer oligonucleotides may comprise one or more modified nucleobase independent of the gapmer pattern of the sugar modifications. Unless otherwise indicated, all modifications are independent of nucleobase sequence.

E. Certain Populations of Modified Oligonucleotides

Populations of modified oligonucleotides in which all of the modified oligonucleotides of the population have the same molecular formula can be stereorandom populations or chirally enriched populations. All of the chiral centers of all of the modified oligonucleotides are stereorandom in a stereorandom population. In a chirally enriched population, at least one particular chiral center is not stereorandom in the modified oligonucleotides of the population. In certain embodiments, the modified oligonucleotides of a chirally enriched population are enriched for β -D ribosyl sugar moieties, and all of the phosphorothioate internucleoside linkages are stereorandom. In certain embodiments, the modified oligonucleotides of a chirally enriched population are enriched for both β -D ribosyl sugar moieties and at least one, particular phosphorothioate internucleoside linkage in a particular stereochemical configuration.

F. Nucleobase Sequence

In certain embodiments, oligonucleotides (or portions thereof) have a nucleobase sequence that is complementary to a second oligonucleotide or an identified reference nucleic acid (or portion thereof), such as a target nucleic acid. In certain embodiments, the nucleobase sequence of a region or entire length of an oligonucleotide is at least 50%, at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or 100% complementary to the second oligonucleotide or identified reference nucleic acid (or portion thereof), such as a target nucleic acid.

II. Certain Oligomeric Compounds

In certain embodiments, provided herein are oligomeric compounds, which comprises an oligonucleotide and optionally one or more conjugate groups and/or terminal groups. A conjugate group consists of a conjugate moiety and a conjugate linker which links the conjugate moiety to the oligonucleotide. Conjugate groups may be attached to either or both ends of an oligonucleotide and/or at any internal position. In certain embodiments, conjugate groups are attached to the 2'-position of a nucleoside of a modified oligonucleotide. In certain embodiments, conjugate groups are attached to either or both ends of an oligonucleotide (such conjugate groups are also terminal groups). In certain such embodiments, conjugate groups or terminal groups are attached at the 3' and/or 5'-end of oligonucleotides.

A. Certain Conjugate Groups

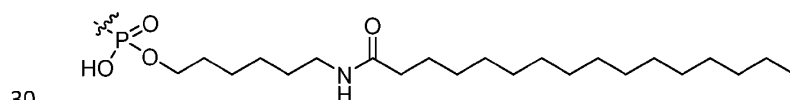
In certain embodiments, oligonucleotides are covalently attached to one or more conjugate groups. In certain embodiments, conjugate groups modify one or more properties of the attached oligonucleotide, including but not limited

to pharmacodynamics, pharmacokinetics, stability, binding, absorption, tissue distribution, cellular distribution, cellular uptake, charge and clearance.

In certain embodiments, conjugation of one or more carbohydrate moieties to a modified oligonucleotide can alter one or more properties of the modified oligonucleotide. In certain embodiments, the carbohydrate moiety is attached to a modified subunit of the modified oligonucleotide. For example, the ribose sugar of one or more ribonucleotide subunits of a modified oligonucleotide can be replaced with another moiety, e.g. a non-carbohydrate (preferably cyclic) carrier to which is attached a carbohydrate ligand. A ribonucleotide subunit in which the ribose sugar of the subunit has been so replaced is referred to herein as a ribose replacement modification subunit (RRMS), which is a modified sugar moiety. A cyclic carrier may be a carbocyclic ring system, i.e., one or more ring atoms may be a heteroatom, e.g., nitrogen, oxygen, sulphur. The cyclic carrier may be a monocyclic ring system, or may contain two or more rings, e.g. fused rings. The cyclic carrier may be a fully saturated ring system, or it may contain one or more double bonds. In certain embodiments, the modified oligonucleotide is a gapmer.

In certain embodiments, conjugate groups impart a new property on the attached oligonucleotide, e.g., fluorophores or reporter groups that enable detection of the oligonucleotide. Certain conjugate groups and conjugate moieties have been described previously, for example: cholesterol moiety (Letsinger et al., *Proc. Natl. Acad. Sci. USA*, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Lett.*, 1994, 4, 1053-1060), a thioether, e.g., hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci.*, 1992, 660, 306-309; Manoharan et al., *Bioorg. Med. Chem. Lett.*, 1993, 3, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucleic Acids Res.*, 1992, 20, 533-538), an aliphatic chain, e.g., do-decan-diol or undecyl residues (Saison-Behmoaras et al., *EMBO J.*, 1991, 10, 1111-1118; Kabanov et al., *FEBS Lett.*, 1990, 259, 327-330; Svinarchuk et al., *Biochimie*, 1993, 75, 49-54), a phospholipid, e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett.*, 1995, 36, 3651-3654; Shea et al., *Nucleic Acids Res.*, 1990, 18, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., *Nucleosides & Nucleotides*, 1995, 14, 969-973), or adamantane acetic acid a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, 1264, 229-237), an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.*, 1996, 277, 923-937), a tocopherol group (Nishina et al., *Molecular Therapy Nucleic Acids*, 2015, 4, e220; and Nishina et al., *Molecular Therapy*, 2008, 16, 734-740), or a GalNAc cluster (e.g., WO2014/179620).

In certain embodiments, a conjugate group consists of a lipid and a conjugate linker. In certain embodiments, a conjugate group is a phosphate linked lipid having the following structure:



1. Conjugate Moieties

Conjugate moieties include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates (e.g., GalNAc), antibodies, vitamin moieties, polyethylene glycols, thioethers, polyethers, cholesterol, thiocholesterols, cholic acid moieties, folate, lipids, phospholipids, biotin, phenazine, phenanthridine, anthraquinone, adamantane, acridine, fluoresceins, rhodamines, coumarins, fluorophores, and dyes.

In certain embodiments, a conjugate moiety comprises an active drug substance, for example, aspirin, warfarin, phenylbutazone, ibuprofen, suprofen, fen-bufen, ketoprofen, (S)-(+)-pranoprofen, carprofen, dansylsarcosine, 2,3,5-triodobenzoic acid, fingolimod, flufenamic acid, folinic acid, a benzothiadiazide, chlorothiazide, a diazepam, indo-methicin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

5 In certain embodiments, conjugate moieties are selected from any of C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

10 In certain embodiments, conjugate moieties are selected from any of C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, or C5 alkyl, where the alkyl chain has one or more unsaturated bonds.

2. Conjugate Linkers

15 Conjugate moieties are attached to oligonucleotides through conjugate linkers. In certain oligomeric compounds, the conjugate linker is a single chemical bond (i.e., the conjugate moiety is attached directly to an oligonucleotide through a single bond). In certain embodiments, the conjugate linker comprises a chain structure, such as a hydrocarbyl chain, or an oligomer of repeating units such as ethylene glycol, nucleosides, or amino acid units.

In certain embodiments, a conjugate linker comprises pyrrolidine.

20 In certain embodiments, a conjugate linker comprises one or more groups selected from alkyl, amino, oxo, amide, disulfide, polyethylene glycol, ether, thioether, and hydroxylamino. In certain such embodiments, the conjugate linker comprises groups selected from alkyl, amino, oxo, amide and ether groups. In certain embodiments, the conjugate linker comprises groups selected from alkyl and amide groups. In certain embodiments, the conjugate linker comprises groups selected from alkyl and ether groups. In certain embodiments, the conjugate linker comprises at least one
25 phosphorus moiety. In certain embodiments, the conjugate linker comprises at least one phosphate group. In certain embodiments, the conjugate linker includes at least one neutral linking group.

In certain embodiments, conjugate linkers, including the conjugate linkers described above, are bifunctional linking moieties, *e.g.*, those known in the art to be useful for attaching conjugate groups to compounds, such as the oligonucleotides provided herein. In general, a bifunctional linking moiety comprises at least two functional groups. One
30 of the functional groups is selected to bind to a particular site on a compound and the other is selected to bind to a conjugate group. Examples of functional groups used in a bifunctional linking moiety include but are not limited to electrophiles for reacting with nucleophilic groups and nucleophiles for reacting with electrophilic groups. In certain embodiments, bifunctional linking moieties comprise one or more groups selected from amino, hydroxyl, carboxylic acid, thiol, alkyl, alkenyl, and alkynyl.

35 Examples of conjugate linkers include but are not limited to pyrrolidine, 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) and 6-aminoheptanoic acid (AHEX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl or substituted or unsubstituted C₂-C₁₀ alkynyl, wherein a nonlimiting list of preferred

substituent groups includes hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl.

In certain embodiments, conjugate linkers comprise 1-10 linker-nucleosides. In certain embodiments, conjugate linkers comprise 2-5 linker-nucleosides. In certain embodiments, conjugate linkers comprise exactly 3 linker-nucleosides. In certain embodiments, conjugate linkers comprise the TCA motif. In certain embodiments, such linker-nucleosides are modified nucleosides. In certain embodiments such linker-nucleosides comprise a modified sugar moiety. In certain embodiments, linker-nucleosides are unmodified. In certain embodiments, linker-nucleosides comprise an optionally protected heterocyclic base selected from a purine, substituted purine, pyrimidine or substituted pyrimidine. In certain embodiments, a cleavable moiety is a nucleoside selected from uracil, thymine, cytosine, 4-N-benzoylcytosine, 5-methylcytosine, 4-N-benzoyl-5-methylcytosine, adenine, 6-N-benzoyladenine, guanine and 2-N-isobutyrylguanine. It is typically desirable for linker-nucleosides to be cleaved from the oligomeric compound after it reaches a target tissue. Accordingly, linker-nucleosides are typically linked to one another and to the remainder of the oligomeric compound through cleavable bonds. In certain embodiments, such cleavable bonds are phosphodiester bonds.

Herein, linker-nucleosides are not considered to be part of the oligonucleotide. Accordingly, in embodiments in which an oligomeric compound comprises an oligonucleotide consisting of a specified number or range of linked nucleosides and/or a specified percent complementarity to a reference nucleic acid and the oligomeric compound also comprises a conjugate group comprising a conjugate linker comprising linker-nucleosides, those linker-nucleosides are not counted toward the length of the oligonucleotide and are not used in determining the percent complementarity of the oligonucleotide for the reference nucleic acid. For example, an oligomeric compound may comprise (1) a modified oligonucleotide consisting of 8-30 nucleosides and (2) a conjugate group comprising 1-10 linker-nucleosides that are contiguous with the nucleosides of the modified oligonucleotide. The total number of contiguous linked nucleosides in such an oligomeric compound is more than 30. Alternatively, an oligomeric compound may comprise a modified oligonucleotide consisting of 8-30 nucleosides and no conjugate group. The total number of contiguous linked nucleosides in such an oligomeric compound is no more than 30. Unless otherwise indicated conjugate linkers comprise no more than 10 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 5 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 3 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 2 linker-nucleosides. In certain embodiments, conjugate linkers comprise no more than 1 linker-nucleoside.

In certain embodiments, it is desirable for a conjugate group to be cleaved from the oligonucleotide. For example, in certain circumstances oligomeric compounds comprising a particular conjugate moiety are better taken up by a particular cell type, but once the oligomeric compound has been taken up, it is desirable that the conjugate group be cleaved to release the unconjugated or parent oligonucleotide. Thus, certain conjugate linkers may comprise one or more cleavable moieties. In certain embodiments, a cleavable moiety is a cleavable bond. In certain embodiments, a cleavable moiety is a group of atoms comprising at least one cleavable bond. In certain embodiments, a cleavable moiety comprises a group of atoms having one, two, three, four, or more than four cleavable bonds. In certain embodiments, a cleavable moiety is selectively cleaved inside a cell or subcellular compartment, such as a lysosome. In certain embodiments, a cleavable moiety is selectively cleaved by endogenous enzymes, such as nucleases.

In certain embodiments, a cleavable bond is selected from among: an amide, an ester, an ether, one or both esters of a phosphodiester, a phosphate ester, a carbamate, or a disulfide. In certain embodiments, a cleavable bond is

one or both of the esters of a phosphodiester. In certain embodiments, a cleavable moiety comprises a phosphate or phosphodiester. In certain embodiments, the cleavable moiety is a phosphate linkage between an oligonucleotide and a conjugate moiety or conjugate group.

5 In certain embodiments, a cleavable moiety comprises or consists of one or more linker-nucleosides. In certain such embodiments, the one or more linker-nucleosides are linked to one another and/or to the remainder of the oligomeric compound through cleavable bonds. In certain embodiments, such cleavable bonds are unmodified phosphodiester bonds. In certain embodiments, a cleavable moiety is 2'-deoxynucleoside that is attached to either the 3' or 5'-terminal nucleoside of an oligonucleotide by a phosphate internucleoside linkage and covalently attached to the remainder of the conjugate linker or conjugate moiety by a phosphate or phosphorothioate linkage. In certain such
10 embodiments, the cleavable moiety is 2'-deoxyadenosine.

3. Cell-Targeting Moieties

In certain embodiments, a conjugate group comprises a cell-targeting moiety. In certain embodiments, the cell-targeting moiety targets neurons. In certain embodiments, the cell-targeting moiety targets a neurotransmitter receptor.
15 In certain embodiments, the cell targeting moiety targets a neurotransmitter transporter. In certain embodiments, the cell targeting moiety targets a GABA transporter. See e.g., WO 2011/131693, WO 2014/064257.

In certain embodiments, conjugate groups comprise cell-targeting moieties that have affinities for transferrin receptor (TfR) (also referred to herein as TfR1 and CD71). In certain embodiments, a conjugate group described herein comprises an anti-TfR1 antibody or fragment thereof. In certain embodiments, the conjugate group comprises a protein
20 or peptide capable of binding TfR1. In certain embodiments, the conjugate group comprises an aptamer capable of binding TfR1. In certain embodiments, the anti-TfR1 antibody or fragment thereof can be any known in the art including but not limited to those described in WO1991/004753; WO2013/103800; WO2014/144060; WO2016/081643; WO2016/179257; WO2016/207240; WO2017/221883; WO2018/129384; WO2018/124121; WO2019/151539; WO2020/132584; WO2020/028864; US 7,208,174; US 9,034,329; and US 10,550,188. In certain embodiments, a
25 fragment of an anti-TfR1 antibody is F(ab')₂, Fab, Fab', Fv, or scFv.

In certain embodiments, the conjugate group comprises a protein or peptide capable of binding TfR1. In certain embodiments, the protein or peptide capable of binding TfR1 can be any known in the art including but not limited to those described in WO2019/140050; WO2020/037150; WO2020/124032; and US 10,138,483.

In certain embodiments, the conjugate group comprises an aptamer capable of binding TfR1. In certain
30 embodiments, the aptamer capable of binding TfR1 can be any known in the art including but not limited to those described in WO2013/163303; WO2019/033051; and WO2020/245198.

B. Certain Terminal Groups

In certain embodiments, oligomeric compounds comprise one or more terminal groups. In certain such
35 embodiments, oligomeric compounds comprise a stabilized 5'-phosphate. Stabilized 5'-phosphates include, but are not limited to 5'-phosphonates, including, but not limited to 5'-vinylphosphonates. In certain embodiments, terminal groups comprise one or more abasic sugar moieties and/or inverted nucleosides. In certain embodiments, a terminal group comprises an inverted abasic sugar moiety. In certain embodiments, the inverted abasic sugar moiety may be further attached to a conjugate group. In certain embodiments, terminal groups comprise one or more 2'-linked nucleosides or

sugar moieties. In certain such embodiments, the 2'-linked group is an abasic sugar moiety. Such terminal abasic sugar moieties can be attached to either or both ends of an oligonucleotide.

III. Antisense Activity

5 In certain embodiments, oligomeric compounds are capable of hybridizing to a target nucleic acid, resulting in at least one antisense activity. In certain embodiments, an oligomeric compound forms an oligomeric duplex with a second oligomeric compound comprising a complementary nucleobase sequence. Such oligomeric compounds and oligomeric duplexes are antisense compounds. In certain embodiments, antisense compounds are deemed to have antisense activity when they reduce or inhibit the amount or activity of a target nucleic acid by 50% or more in the
10 standard *in vitro* assay. In certain embodiments, antisense compounds selectively affect one or more target nucleic acid. Such antisense compounds comprise a nucleobase sequence that hybridizes to one or more target nucleic acid, resulting in one or more desired antisense activity and does not hybridize to one or more non-target nucleic acid or does not hybridize to one or more non-target nucleic acid in such a way that results in significant undesired antisense activity.

In certain antisense activities, hybridization of an antisense compound to a target nucleic acid results in
15 recruitment of a protein that cleaves the target nucleic acid. For example, certain antisense compounds result in RNase H mediated cleavage of the target nucleic acid. RNase H is a cellular endonuclease that cleaves the RNA strand of an RNA:DNA duplex. The DNA in such an RNA:DNA duplex need not be unmodified DNA. In certain embodiments, described herein are antisense compounds that are sufficiently "DNA-like" to elicit RNase H activity. In certain embodiments, one or more non-DNA-like nucleoside in the gap of a gapmer is tolerated.

20 In certain antisense activities, an antisense compound or a portion of an antisense compound is loaded into an RNA-induced silencing complex (RISC), ultimately resulting in cleavage of the target nucleic acid. For example, certain antisense compounds result in cleavage of the target nucleic acid by Argonaute. Antisense compounds that are loaded into RISC are RNAi agents. RNAi agents may be double-stranded (siRNA or dsRNAi) or single-stranded (ssRNAi).

In certain embodiments, hybridization of an antisense compound to a target nucleic acid does not result in
25 recruitment of a protein that cleaves that target nucleic acid. In certain embodiments, hybridization of the antisense compound to the target nucleic acid results in alteration of splicing of the target nucleic acid. In certain embodiments, hybridization of an antisense compound to a target nucleic acid results in inhibition of a binding interaction between the target nucleic acid and a protein or other nucleic acid. In certain embodiments, hybridization of an antisense compound to a target nucleic acid results in alteration of translation of the target nucleic acid.

30 Antisense activities may be observed directly or indirectly. In certain embodiments, observation or detection of an antisense activity involves observation or detection of a change in an amount of a target nucleic acid or protein encoded by such target nucleic acid, a change in the ratio of splice variants of a nucleic acid or protein and/or a phenotypic change in a cell or subject.

35 IV. Certain Target Nucleic Acids

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid. In certain embodiments, the target nucleic acid is an endogenous RNA molecule. In certain embodiments, the target nucleic acid encodes a protein. In certain such embodiments, the target nucleic acid is selected from: a mature mRNA and a pre-mRNA, including intronic, exonic and untranslated regions. In

certain embodiments, the target RNA is a mature mRNA. In certain embodiments, the target nucleic acid is a pre-mRNA. In certain embodiments, the target region is entirely within an intron. In certain embodiments, the target region spans an intron/exon junction. In certain embodiments, the target region is at least 50% within an intron. In certain embodiments, the target nucleic acid is the RNA transcriptional product of a retrogene. In certain embodiments, the target nucleic acid is a non-coding RNA. In certain embodiments, the target non-coding RNA is selected from: a long non-coding RNA, a short non-coding RNA, an intronic RNA molecule.

A. Complementarity/Mismatches to the Target Nucleic Acid and Duplex Complementarity

In certain embodiments, oligonucleotides are complementary to the target nucleic acid over the entire length of the oligonucleotide. In certain embodiments, oligonucleotides are 99%, 95%, 90%, 85%, or 80% complementary to the target nucleic acid. In certain embodiments, oligonucleotides are at least 80% complementary to the target nucleic acid over the entire length of the oligonucleotide and comprise a region that is 100% or fully complementary to a target nucleic acid. In certain embodiments, the region of full complementarity is from 6 to 20, 10 to 18, or 18 to 20 nucleobases in length.

It is possible to introduce mismatch bases without eliminating activity. For example, Gautschi et al (J. Natl. Cancer Inst. 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bcl-2 mRNA and having 3 mismatches to the bcl-xL mRNA to reduce the expression of both bcl-2 and bcl-xL *in vitro* and *in vivo*. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity *in vivo*. Maher and Dolnick (Nucleic Acids Res. 16:3341-3358, 1988) tested a series of tandem 14 nucleobase oligonucleotides, and 28 and 42 nucleobase oligonucleotides comprised of the sequence of two or three of the tandem oligonucleotides, respectively, for their ability to arrest translation of human DHFR in a rabbit reticulocyte assay. Each of the three 14 nucleobase oligonucleotides alone was able to inhibit translation, albeit at a more modest level than the 28 or 42 nucleobase oligonucleotides.

In certain embodiments, oligonucleotides comprise one or more mismatched nucleobases relative to the target nucleic acid. In certain embodiments, antisense activity against the target is reduced by such mismatch, but activity against a non-target is reduced by a greater amount. Thus, in certain embodiments selectivity of the oligonucleotide is improved.

In certain embodiments, a mismatch is specifically positioned within an oligonucleotide having a gapmer motif. In certain embodiments, the mismatch is at position 1, 2, 3, 4, 5, 6, 7, or 8 from the 5'-end of the gap region. In certain embodiments, the mismatch is at position 9, 8, 7, 6, 5, 4, 3, 2, 1 from the 3'-end of the gap region. In certain embodiments, the mismatch is at position 1, 2, 3, or 4 from the 5'-end of the wing region. In certain embodiments, the mismatch is at position 4, 3, 2, or 1 from the 3'-end of the wing region.

B. SNCA

In certain embodiments, oligomeric compounds described herein comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid, wherein the target nucleic acid is SNCA. In each of the embodiments described above, the oligomeric compounds may target the SNCA nucleic acid. In certain embodiments, the SNCA nucleic acid has the sequence set forth in SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022), SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), SEQ ID NO: 3 (GENBANK

Accession No: NM_001146055.1), SEQ ID NO: 4 (Ensembl ID ENST00000618500.4, Ensembl release 106-Apr 2022), SEQ ID NO: 5 (GENBANK Accession No: NM_000345.3), SEQ ID NO: 6 (GENBANK Accession No: JN709863.1), SEQ ID NO: 7 (GENBANK Accession No: BC013293.2), SEQ ID NO: 8 (GENBANK Accession No:

NM_001146054.2), or SEQ ID NO: 9 (GENBANK Accession No: HQ830269.1). In certain embodiments, contacting a cell with an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 reduces the amount of SNCA RNA, and in certain embodiments reduces the amount of alpha-synuclein protein. In certain embodiments, contacting a cell with an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 results in reduced aggregation of alpha-synuclein protein. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide and a conjugate group.

In certain embodiments, contacting a cell with an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 reduces the amount of SNCA RNA in a cell. In certain embodiments, contacting a cell with an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 reduces the amount of alpha-synuclein protein in the cell. In certain embodiments, the cell is *in vitro*. In certain embodiments, the cell is in a subject. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, contacting a cell in a subject with an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 ameliorates one or more symptoms or hallmarks of a synucleinopathy. In certain embodiments, the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain embodiments, the one or more symptoms or hallmarks include Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, and Alzheimer's disease.

In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of SNCA RNA *in vitro* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vitro* assay. In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of SNCA RNA *in vivo* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vivo* assay. In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of alpha-synuclein protein *in vitro* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vitro* assay. In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of alpha-synuclein protein *in vivo* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vivo* assay. In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of SNCA RNA in the cell of a subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In certain embodiments, an oligomeric compound described herein that is complementary to any of SEQ ID NOs: 1-9 is capable of reducing the amount of alpha-synuclein protein or the amount of alpha-synuclein protein

aggregation in the cell of a subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%.

C. Certain Target Nucleic Acids in Certain Tissues

5 In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid, wherein the target nucleic acid is expressed in a pharmacologically relevant tissue. In certain embodiments, the pharmacologically relevant tissue are the cells and tissues that comprise the central nervous system (CNS). Such tissues include the brain and the spinal cord. In certain embodiments, the pharmacologically relevant tissues include the motor cortex, frontal cortex, caudate, putamen, amygdala, pons, substantia nigra, putamen, cerebellar peduncle, corpus callosum, deep cerebellar nuclei (DCN), entorhinal cortex (Ent
10 Cortex), hippocampus, insular cortex, medulla oblongata, central gray matter, pulvinar, occipital cortex, cerebral cortex, temporal cortex, globus pallidus, superior colliculi, and basal forebrain nuclei. In certain embodiments, the cells are brain cells. In certain embodiments, the cells include neurons and oligodendrocytes.

15 V. Certain Methods and Uses

Certain embodiments provided herein relate to methods of reducing or inhibiting SNCA expression or activity, which can be useful for treating, preventing, or ameliorating a synucleinopathy in a subject. In certain embodiments, the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or
20 Alzheimer's disease.

In certain embodiments, a method comprises administering to a subject an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to a SNCA nucleic acid. In certain embodiments, the subject has or is at risk for developing a synucleinopathy. In certain embodiments, the subject has or is at risk for developing Parkinson's disease, dementia with
25 Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain embodiments, the subject has Parkinson's disease. In certain embodiments, the subject has dementia with Lewy bodies (DLB). In certain embodiments, the subject has diffuse Lewy body disease. In certain embodiments, the subject has Parkinson's disease dementia (PDD). In certain embodiments, the subject has pure autonomic failure. In certain embodiments, the subject
30 has multiple system atrophy (MSA). In certain embodiments, the subject has neuronopathic Gaucher's disease. In certain embodiments, the subject has Alzheimer's disease.

In certain embodiments, a method for treating a synucleinopathy comprises administering to a subject an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to a SNCA nucleic acid. In certain embodiments, the subject has or is at risk for
35 developing a synucleinopathy. In certain embodiments, the subject has or is at risk for developing Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain embodiments, the subject has Parkinson's disease. In certain embodiments, the subject has multiple system atrophy (MSA). In certain embodiments, the subject has Alzheimer's disease. In certain embodiments, at least one symptom or

hallmark of the synucleinopathy is ameliorated. In certain embodiments, the at least one symptom or hallmark is motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.

5 In certain embodiments, a method of reducing expression of SNCA, for example RNA, or reducing the expression of alpha-synuclein protein in a cell comprises contacting the cell with an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to a SNCA nucleic acid. In certain embodiments, the subject has or is at risk for developing a synucleinopathy. In certain embodiments, the subject has or is at risk for developing Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease. In certain embodiments, the subject has Parkinson's disease. In certain embodiments, the subject has multiple system atrophy (MSA). In certain
10 embodiments, the subject has Alzheimer's disease. In certain embodiments, the cell is a brain cell. In certain embodiments, the cell is a neuron. In certain embodiments, the cell is an oligodendrocyte. In certain embodiments, the cell is a human cell.

15 Certain embodiments are drawn to an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to a SNCA nucleic acid, for use in treating a synucleinopathy or for use in the manufacturing of a medicament for treating a synucleinopathy. In certain embodiments, the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic
20 Gaucher's disease, or Alzheimer's disease.

In any of the methods or uses described herein, the oligomeric compound, the modified oligonucleotide, the oligomeric duplex, or the antisense agent can be any described herein.

VI. Certain Pharmaceutical Compositions

25 In certain embodiments, described herein are pharmaceutical compositions comprising one or more oligomeric compounds. In certain embodiments, the one or more oligomeric compounds each consists of a modified oligonucleotide. In certain embodiments, the pharmaceutical composition comprises a pharmaceutically acceptable diluent or carrier. In certain embodiments, a pharmaceutical composition comprises or consists of a sterile saline solution and one or more oligomeric compound. In certain embodiments, the sterile saline is pharmaceutical grade
30 saline. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and sterile water. In certain embodiments, the sterile water is pharmaceutical grade water. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and phosphate-buffered saline (PBS). In certain embodiments, the sterile PBS is pharmaceutical grade PBS. In certain embodiments, a pharmaceutical composition comprises or consists of one or more oligomeric compound and artificial cerebrospinal fluid
35 ("artificial CSF" or "aCSF"). In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

In certain embodiments, a pharmaceutical composition comprises a modified oligonucleotide and artificial cerebrospinal fluid (aCSF). In certain embodiments, a pharmaceutical composition consists of a modified oligonucleotide and artificial cerebrospinal fluid. In certain embodiments, a pharmaceutical composition consists

essentially of a modified oligonucleotide and artificial cerebrospinal fluid. In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

In certain embodiments, aCSF comprises sodium chloride, potassium chloride, sodium dihydrogen phosphate dihydrate, sodium phosphate dibasic anhydrous, calcium chloride dihydrate, and magnesium chloride hexahydrate. In certain embodiments, the pH of an aCSF solution is modulated with a suitable pH-adjusting agent, for example, with acids such as hydrochloric acid and alkalis such as sodium hydroxide, to a range of from about 7.1-7.3, or to about 7.2.

In certain embodiments, pharmaceutical compositions comprise one or more oligomeric compound and one or more excipients. In certain embodiments, excipients are selected from water, salt solutions, alcohol, polyethylene glycols, gelatin, lactose, amylase, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose and polyvinylpyrrolidone.

In certain embodiments, oligomeric compounds may be admixed with pharmaceutically acceptable active and/or inert substances for the preparation of pharmaceutical compositions or formulations. Compositions and methods for the formulation of pharmaceutical compositions depend on a number of criteria, including, but not limited to, route of administration, extent of disease, or dose to be administered.

In certain embodiments, pharmaceutical compositions comprising an oligomeric compound encompass any pharmaceutically acceptable salts of the oligomeric compound, esters of the oligomeric compound, or salts of such esters. In certain embodiments, pharmaceutical compositions comprising oligomeric compounds comprising one or more oligonucleotide, upon administration to a subject, including a human, are capable of providing (directly or indirectly) the biologically active metabolite or residue thereof. Accordingly, for example, the disclosure is also drawn to pharmaceutically acceptable salts of oligomeric compounds, prodrugs, pharmaceutically acceptable salts of such prodrugs, and other bioequivalents. In certain embodiments, pharmaceutically acceptable salts comprise inorganic salts, such as monovalent or divalent inorganic salts. Suitable pharmaceutically acceptable salts include, but are not limited to, sodium, potassium, calcium, and magnesium salts. In certain embodiments, prodrugs comprise one or more conjugate group attached to an oligonucleotide, wherein the conjugate group is cleaved by endogenous nucleases within the body.

In certain embodiments, oligomeric compounds are lyophilized and isolated as sodium salts. In certain embodiments, the sodium salt of an oligomeric compound is mixed with a pharmaceutically acceptable diluent. In certain embodiments, the pharmaceutically acceptable diluent comprises sterile saline, sterile water, PBS, or aCSF. In certain embodiments, the sodium salt of an oligomeric compound is mixed with PBS. In certain embodiments, the sodium salt of an oligomeric compound is mixed with aCSF.

Lipid moieties have been used in nucleic acid therapies in a variety of methods. In certain such methods, the nucleic acid, such as an oligomeric compound, is introduced into preformed liposomes or lipoplexes made of mixtures of cationic lipids and neutral lipids. In certain methods, DNA complexes with mono- or poly-cationic lipids are formed without the presence of a neutral lipid. In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to a particular cell or tissue. In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to fat tissue. In certain embodiments, a lipid moiety is selected to increase distribution of a pharmaceutical agent to muscle tissue.

In certain embodiments, pharmaceutical compositions comprise a delivery system. Examples of delivery systems include, but are not limited to, liposomes and emulsions. Certain delivery systems are useful for preparing

certain pharmaceutical compositions including those comprising hydrophobic compounds. In certain embodiments, certain organic solvents such as dimethylsulfoxide are used.

In certain embodiments, pharmaceutical compositions comprise one or more tissue-specific delivery molecules designed to deliver the one or more pharmaceutical agents of the present invention to specific tissues or cell types. For example, in certain embodiments, pharmaceutical compositions include liposomes coated with a tissue-specific antibody.

In certain embodiments, pharmaceutical compositions comprise a co-solvent system. Certain of such co-solvent systems comprise, for example, benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. In certain embodiments, such co-solvent systems are used for hydrophobic compounds. A non-limiting example of such a co-solvent system is the VPD co-solvent system, which is a solution of absolute ethanol comprising 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant Polysorbate 80™ and 65% w/v polyethylene glycol 300. The proportions of such co-solvent systems may be varied considerably without significantly altering their solubility and toxicity characteristics. Furthermore, the identity of co-solvent components may be varied: for example, other surfactants may be used instead of Polysorbate 80™; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, e.g., polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose.

In certain embodiments, pharmaceutical compositions are prepared for oral administration. In certain embodiments, pharmaceutical compositions are prepared for buccal administration. In certain embodiments, a pharmaceutical composition is prepared for administration by injection (e.g., intravenous, subcutaneous, intramuscular, intrathecal (IT), intracerebroventricular (ICV), etc.). In certain of such embodiments, a pharmaceutical composition comprises a carrier and is formulated in aqueous solution, such as water or physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. In certain embodiments, other ingredients are included (e.g., ingredients that aid in solubility or serve as preservatives). In certain embodiments, injectable suspensions are prepared using appropriate liquid carriers, suspending agents and the like. Certain pharmaceutical compositions for injection are presented in unit dosage form, e.g., in ampoules or in multi-dose containers. Certain pharmaceutical compositions for injection are suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Certain solvents suitable for use in pharmaceutical compositions for injection include, but are not limited to, lipophilic solvents and fatty oils, such as sesame oil, synthetic fatty acid esters, such as ethyl oleate or triglycerides, and liposomes.

Under certain conditions, certain compounds disclosed herein act as acids. Although such compounds may be drawn or described in protonated (free acid) form, or ionized and in association with a cation (salt) form, aqueous solutions of such compounds exist in equilibrium among such forms. For example, a phosphodiester linkage of an oligonucleotide in aqueous solution exists in equilibrium among free acid, anion and salt forms. Unless otherwise indicated, compounds described herein are intended to include all such forms. Moreover, certain oligonucleotides have several such linkages, each of which is in equilibrium. Thus, oligonucleotides in solution exist in an ensemble of forms at multiple positions all at equilibrium. The term "oligonucleotide" is intended to include all such forms. Drawn structures necessarily depict a single form. Nevertheless, unless otherwise indicated, such drawings are likewise intended to include corresponding forms. Herein, a structure depicting the free acid of a compound followed by the term "or a pharmaceutically acceptable salt thereof" expressly includes all such forms that may be fully or partially

protonated/de-protonated/in association with a cation or a combination of cations. In certain embodiments, one or more specific cation is identified. The cations include, but are not limited to, sodium, potassium, calcium, and magnesium. In certain embodiments, a structure depicting the free acid of a compound followed by the term “or a pharmaceutically acceptable salt thereof” expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with one or more cations selected from sodium, potassium, calcium, and magnesium.

In certain embodiments, modified oligonucleotides or oligomeric compounds are in aqueous solution with sodium. In certain embodiments, modified oligonucleotides or oligomeric compounds are in aqueous solution with potassium. In certain embodiments, modified oligonucleotides or oligomeric compounds are in PBS. In certain embodiments, modified oligonucleotides or oligomeric compounds are in water. In certain such embodiments, the pH of the solution is adjusted with NaOH and/or HCl to achieve a desired pH.

Herein, certain specific doses are described. A dose may be in the form of a dosage unit. For clarity, a dose (or dosage unit) of a modified oligonucleotide or an oligomeric compound in milligrams indicates the mass of the free acid form of the modified oligonucleotide or oligomeric compound. As described above, in aqueous solution, the free acid is in equilibrium with anionic and salt forms. However, for the purpose of calculating dose, it is assumed that the modified oligonucleotide or oligomeric compound exists as a solvent-free, sodium-acetate free, anhydrous, free acid.

In certain embodiments, where a modified oligonucleotide or an oligomeric compound is in solution comprising sodium (e.g., saline), the modified oligonucleotide or oligomeric compound may be partially or fully de-protonated and in association with sodium ions. However, the mass of the protons is nevertheless counted toward the weight of the dose, and the mass of the sodium ions is not counted toward the weight of the dose. Thus, for example, a dose, or dosage unit, of 10 mg of Compound No. 1482139 equals the number of fully protonated molecules that weighs 10 mg. This would be equivalent to 10.61 mg of solvent-free, sodium acetate-free, anhydrous sodiated Compound No. 1482139.

In certain embodiments, where a modified oligonucleotide or oligomeric compound is in a solution, such as aCSF, comprising sodium, potassium, calcium, and magnesium, the modified oligonucleotide or oligomeric compound may be partially or fully de-protonated and in association with sodium, potassium, calcium, and/or magnesium. However, the mass of the protons is nevertheless counted toward the weight of the dose, and the mass of the sodium, potassium, calcium, and magnesium ions is not counted toward the weight of the dose.

In certain embodiments, when an oligomeric compound comprises a conjugate group, the mass of the conjugate group may be included in calculating the dose of such oligomeric compound. If the conjugate group also has an acid, the conjugate group is likewise assumed to be fully protonated for the purpose of calculating dose.

VII. Certain Oligomeric Compounds

In certain embodiments, an oligomeric compound disclosed herein comprises a modified oligonucleotide consisting of 12 to 50 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide comprises at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 13-3334. In certain such embodiments, the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage. In certain embodiments, the oligomeric compound comprises a conjugate group. In certain embodiments, the oligomeric

compound does not comprise a conjugate group. In certain embodiments, the oligomeric compound comprises a terminal group. In certain embodiments, the oligomeric compound does not comprise a terminal group.

In certain embodiments, an oligomeric compound disclosed herein comprises a modified oligonucleotide consisting of 12 to 50 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide comprises at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of 5'-ACAGATATTTTGTCTGCC-3' (SEQ ID NO: 3318). In certain embodiments, the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage. In certain embodiments, the modified sugar moiety is a non-bicyclic modified sugar moiety selected from a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, a 2'-β-D-deoxyxylosyl sugar moiety, and a 2'-α-L-deoxyribose sugar moiety. In certain embodiments, the modified internucleoside linkage is selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, the oligomeric compound comprises a conjugate group. In certain embodiments, the oligomeric compound does not comprise a conjugate group. In certain embodiments, the oligomeric compound comprises a terminal group. In certain embodiments, the oligomeric compound does not comprise a terminal group.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3318. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeeeeeeeeeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, the modified oligonucleotide comprises a modified internucleoside linkage selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3318. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeeeeeeeeeeee, wherein each "c" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, the modified oligonucleotide has a modified internucleoside linkage motif of (from 5' to 3') ssssszzzzssssssss, wherein each "s" is a phosphorothioate internucleoside linkage and each "z" is a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3318. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeeeeeeeeeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, the modified oligonucleotide has a modified internucleoside linkage motif of (from 5' to 3') ssssszzzzssssssss, wherein each "s" is a phosphorothioate internucleoside linkage and each "z" is a mesyl

phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

5 In certain embodiments, an oligomeric compound disclosed herein comprises a modified oligonucleotide consisting of 12 to 50 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide comprises at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of 5'-ACGACATTTTCTTGCCTCTT-3' (SEQ ID NO: 3319). In certain embodiments, the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage. In 10 certain embodiments, the modified sugar moiety is a non-bicyclic modified sugar moiety selected from a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, a 2'-β-D-deoxyxylosyl sugar moiety, and a 2'-α-L-deoxyribosyl sugar moiety. In certain embodiments, the modified internucleoside linkage is selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified 15 oligonucleotide is a modified nucleobase. In certain embodiments, the oligomeric compound comprises a conjugate group. In certain embodiments, the oligomeric compound does not comprise a conjugate group. In certain embodiments, the oligomeric compound comprises a terminal group. In certain embodiments, the oligomeric compound does not comprise a terminal group.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3319. In 20 certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeddddddddeeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribosyl sugar moiety. In certain embodiments, the modified oligonucleotide comprises a modified internucleoside linkage selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at 25 least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3319. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') 30 eeeeddddddddeeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribosyl sugar moiety. In certain embodiments, the modified oligonucleotide has a modified internucleoside linkage motif of (from 5' to 3') ssooszssssszssoss, wherein each "s" is a phosphorothioate internucleoside linkage, each "o" is a phosphodiester internucleoside linkage, and each "z" is a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one 35 nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, an oligomeric compound disclosed herein comprises a modified oligonucleotide consisting of 12 to 50 linked nucleosides, wherein the nucleobase sequence of the modified oligonucleotide comprises at

least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of 5'-ATCACGACATTTTCTTGCCCT-3' (SEQ ID NO: 3328). In certain embodiments, the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage. In certain embodiments, the modified sugar moiety is a non-bicyclic modified sugar moiety selected from a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, a 2'-β-D-deoxyxylosyl sugar moiety, and a 2'-α-L-deoxyribose sugar moiety. In certain embodiments, the modified internucleoside linkage is selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, the oligomeric compound comprises a conjugate group. In certain embodiments, the oligomeric compound does not comprise a conjugate group. In certain embodiments, the oligomeric compound comprises a terminal group. In certain embodiments, the oligomeric compound does not comprise a terminal group.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3328. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeeeddddddddeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, the modified oligonucleotide comprises a modified internucleoside linkage selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, the modified oligonucleotide has a nucleobase sequence of SEQ ID NO: 3328. In certain embodiments, the modified oligonucleotide has a modified sugar motif of (from 5' to 3') eeeeeeddddddddeeee, wherein each "e" is a 2'-MOE sugar moiety and each "d" is a 2'-β-D-deoxyribose sugar moiety. In certain embodiments, the modified oligonucleotide has a modified internucleoside linkage motif of (from 5' to 3') soooooosssssssoss, wherein each "s" is a phosphorothioate internucleoside linkage and each "o" is a phosphodiester internucleoside linkage. In certain embodiments, each nucleobase of the modified oligonucleotide is an unmodified nucleobase. In certain embodiments, at least one nucleobase of the modified oligonucleotide is a modified nucleobase. In certain embodiments, at least one cytosine of the modified oligonucleotide is a modified cytosine. In certain embodiments, each cytosine of the modified oligonucleotide is a 5-methylcytosine.

In certain embodiments, disclosed herein is an oligomeric compound according to the following chemical notation: $N^1_{es}{}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{dz}T_{dz}T_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^mC_{es}T_{es}G_{es}{}^mC_{es}N^2_e$ (SEQ ID NO: 3346), wherein:

- A = an adenine nucleobase,
- mC = a 5-methylcytosine nucleobase,
- G = a guanine nucleobase,
- T = a thymine nucleobase,
- N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,
- N^2 = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein

when N² is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

5 z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group. In certain embodiments, N¹ is an adenine nucleobase. In certain embodiments, N¹ is an unmodified adenine. In certain embodiments, N¹ is a modified adenine. In certain embodiments, N¹ is a hypoxanthine. In certain embodiments, N¹ is an abasic sugar moiety. In certain
 10 embodiments, N¹ is a terminal group. In certain embodiments, N¹ is absent. In certain embodiments, N² is a modified cytosine. In certain embodiments, N² is 5-methylcytosine. In certain embodiments, N² is an unmodified cytosine. In certain
 15 embodiments, N² is an abasic sugar moiety. In certain embodiments, N² is a terminal group. In certain embodiments, N² is absent. In certain embodiments, N³ is a modified thymine. In certain embodiments, N³ is an unmodified thymine. In certain embodiments, N³ is an abasic sugar moiety. In certain embodiments, N³ is a terminal
 20 group. In certain embodiments, N³ is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a modified cytosine. In certain embodiments, N¹ is an adenine nucleobase and N² is an
 25 abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N² is a terminal group. In certain embodiments, N¹ is an adenine nucleobase and N² is absent. In certain embodiments, N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments,
 30 N¹ is a modified adenine and N² is a modified cytosine. In certain embodiments, N¹ is a modified adenine and N² is 5-methylcytosine. In certain embodiments, N¹ is a modified adenine and N² is an abasic sugar moiety. In certain
 35 embodiments, N¹ is a modified adenine and N² is a terminal group. In certain embodiments, N¹ is a modified adenine and N² is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a modified
 40 cytosine. In certain embodiments, N¹ is a hypoxanthine and N² is 5-methylcytosine. In certain embodiments, N¹ is a hypoxanthine and N² is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N² is a terminal group. In certain embodiments, N¹ is a hypoxanthine and N² is absent. In certain embodiments, N¹ is an abasic sugar moiety and
 45 N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain
 50 embodiments, N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is a cytosine nucleobase, a modified cytosine,
 55 an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is absent. In certain
 60 embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety,
 65 a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase. In
 70 certain embodiments, N¹ is an adenine nucleobase and N³ is a modified thymine. In certain embodiments, N¹ is an
 75 adenine nucleobase and N³ is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N³ is a
 80 terminal group. In certain embodiments, N¹ is an adenine nucleobase and N³ is absent. In certain embodiments, N¹ is a
 85 modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is
 90 absent. In certain embodiments, N¹ is a modified adenine and N³ is an unmodified thymine. In certain embodiments, N¹
 95 is a modified adenine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a modified adenine and N³ is a

- terminal group. In certain embodiments, N¹ is a modified adenine and N³ is absent. In certain embodiments, N¹ is a hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N³ is an unmodified thymine. In certain embodiments, N¹ is a hypoxanthine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N³ is a terminal group.
- 5 In certain embodiments, N¹ is a hypoxanthine and N³ is absent. In certain embodiments, N¹ is an abasic sugar moiety and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is absent.
- 10 In certain embodiments, disclosed herein is an oligomeric compound according to the following chemical notation: N¹_{es}^mC_{es}G_{eo}A_{eo}^mC_{es}A_{dz}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{dz}G_{ds}^mC_{ds}T_{eo}^mC_{es}T_{es}N³_e (SEQ ID NO: 3347), wherein:
- A = an adenine nucleobase,
^mC = a 5-methylcytosine nucleobase,
 G = a guanine nucleobase,
 15 T = a thymine nucleobase,
 N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,
 N³ = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N³ is absent its sugar is also absent,
- 20 e = a 2'-MOE sugar moiety,
 d = a 2'-β-D-deoxyribosyl sugar moiety,
 s = a phosphorothioate internucleoside linkage,
 z = a mesyl phosphoramidate internucleoside linkage, and
 o = a phosphodiester internucleoside linkage; and
- 25 wherein the oligomeric compound optionally comprises a conjugate group. In certain embodiments, N¹ is an adenine nucleobase. In certain embodiments, N¹ is an unmodified adenine. In certain embodiments, N¹ is a modified adenine. In certain embodiments, N¹ is a hypoxanthine. In certain embodiments, N¹ is an abasic sugar moiety. In certain embodiments, N¹ is a terminal group. In certain embodiments, N¹ is absent. In certain embodiments, N² is a modified cytosine. In certain embodiments, N² is 5-methylcytosine. In certain embodiments, N² is an unmodified cytosine. In certain embodiments, N² is an abasic sugar moiety. In certain embodiments, N² is a terminal group. In certain
- 30 embodiments, N² is absent. In certain embodiments, N³ is a modified thymine. In certain embodiments, N³ is an unmodified thymine. In certain embodiments, N³ is an abasic sugar moiety. In certain embodiments, N³ is a terminal group. In certain embodiments, N³ is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a modified cytosine. In certain embodiments, N¹ is an adenine nucleobase and N² is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N² is a terminal group. In certain
- 35 embodiments, N¹ is an adenine nucleobase and N² is absent. In certain embodiments, N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a modified adenine and N² is a modified cytosine. In certain embodiments, N¹ is a modified adenine and N² is 5-

methylcytosine. In certain embodiments, N¹ is a modified adenine and N² is an abasic sugar moiety. In certain
 embodiments, N¹ is a modified adenine and N² is a terminal group. In certain embodiments, N¹ is a modified adenine and
 N² is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an
 abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a modified
 5 cytosine. In certain embodiments, N¹ is a hypoxanthine and N² is 5-methylcytosine. In certain embodiments, N¹ is a
 hypoxanthine and N² is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N² is a terminal group.
 In certain embodiments, N¹ is a hypoxanthine and N² is absent. In certain embodiments, N¹ is an abasic sugar moiety and
 N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain
 10 embodiments, N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a
 terminal group, or is absent. In certain embodiments, N¹ is absent and N² is a cytosine nucleobase, a modified cytosine,
 an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is absent. In certain
 embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety,
 a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase. In
 certain embodiments, N¹ is an adenine nucleobase and N³ is a modified thymine. In certain embodiments, N¹ is an
 15 adenine nucleobase and N³ is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N³ is a
 terminal group. In certain embodiments, N¹ is an adenine nucleobase and N³ is absent. In certain embodiments, N¹ is a
 modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is
 absent. In certain embodiments, N¹ is a modified adenine and N³ is an unmodified thymine. In certain embodiments, N¹
 is a modified adenine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a modified adenine and N³ is a
 20 terminal group. In certain embodiments, N¹ is a modified adenine and N³ is absent. In certain embodiments, N¹ is a
 hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is
 absent. In certain embodiments, N¹ is a hypoxanthine and N³ is an unmodified thymine. In certain embodiments, N¹ is a
 hypoxanthine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N³ is a terminal group.
 In certain embodiments, N¹ is a hypoxanthine and N³ is absent. In certain embodiments, N¹ is an abasic sugar moiety and
 25 N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain
 embodiments, N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a
 terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is a thymine nucleobase, a modified thymine,
 an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is absent.

In certain embodiments, disclosed herein is an oligomeric compound according to the following chemical
 30 notation: N¹_{es}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{cs}T_{ds}T_{ds}T_{dz}G_{dz}T_{cs}T_{ds}^mC_{es}T_{es}G_{es}^mC_{es}N²_e (SEQ ID NO: 3348), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

35 N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is
 absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,

N² = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein
 when N² is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribose sugar moiety,

s = a phosphorothioate internucleoside linkage, and

z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group. In certain embodiments, N¹ is an adenine nucleobase. In certain embodiments, N¹ is an unmodified adenine. In certain embodiments, N¹ is a modified adenine. In certain embodiments, N¹ is a hypoxanthine. In certain embodiments, N¹ is an abasic sugar moiety. In certain embodiments, N¹ is a terminal group. In certain embodiments, N¹ is absent. In certain embodiments, N² is a modified cytosine. In certain embodiments, N² is 5-methylcytosine. In certain embodiments, N² is an unmodified cytosine. In certain embodiments, N² is an abasic sugar moiety. In certain embodiments, N² is a terminal group. In certain
 5 embodiments, N² is absent. In certain embodiments, N³ is a modified thymine. In certain embodiments, N³ is an unmodified thymine. In certain embodiments, N³ is an abasic sugar moiety. In certain embodiments, N³ is a terminal group. In certain embodiments, N³ is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a modified cytosine. In certain embodiments, N¹ is an adenine nucleobase and N² is an
 10 abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N² is a terminal group. In certain embodiments, N¹ is an adenine nucleobase and N² is absent. In certain embodiments, N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a modified adenine and N² is a modified cytosine. In certain embodiments, N¹ is a modified adenine and N² is 5-methylcytosine. In certain embodiments, N¹ is a modified adenine and N² is an abasic sugar moiety. In certain
 20 embodiments, N¹ is a modified adenine and N² is a terminal group. In certain embodiments, N¹ is a modified adenine and N² is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a modified cytosine. In certain embodiments, N¹ is a hypoxanthine and N² is 5-methylcytosine. In certain embodiments, N¹ is a hypoxanthine and N² is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N² is a terminal group.
 25 In certain embodiments, N¹ is a hypoxanthine and N² is absent. In certain embodiments, N¹ is an abasic sugar moiety and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is absent. In certain
 30 embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase. In certain embodiments, N¹ is an adenine nucleobase and N³ is a modified thymine. In certain embodiments, N¹ is an adenine nucleobase and N³ is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N³ is a terminal group. In certain embodiments, N¹ is an adenine nucleobase and N³ is absent. In certain embodiments, N¹ is a modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is
 35 absent. In certain embodiments, N¹ is a modified adenine and N³ is an unmodified thymine. In certain embodiments, N¹ is a modified adenine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a modified adenine and N³ is a terminal group. In certain embodiments, N¹ is a modified adenine and N³ is absent. In certain embodiments, N¹ is a hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is

absent. In certain embodiments, N¹ is a hypoxanthine and N³ is an unmodified thymine. In certain embodiments, N¹ is a hypoxanthine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N³ is a terminal group. In certain embodiments, N¹ is a hypoxanthine and N³ is absent. In certain embodiments, N¹ is an abasic sugar moiety and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain
 5 embodiments, N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is absent.

In certain embodiments, disclosed herein is an oligomeric compound according to the following chemical notation: N¹_{es}T_{eo}^mC_{eo}A_{eo}^mC_{eo}G_{eo}A_{ds}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{ds}G_{eo}^mC_{es}^mC_{es}N³_e (SEQ ID NO: 3349), wherein:

10 A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

15 N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,

N³ = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N³ is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

20 s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group. In certain embodiments, N¹ is an adenine nucleobase. In certain embodiments, N¹ is an unmodified adenine. In certain embodiments, N¹ is a modified adenine. In certain embodiments, N¹ is a hypoxanthine. In certain embodiments, N¹ is an abasic sugar moiety. In certain
 25 embodiments, N¹ is a terminal group. In certain embodiments, N¹ is absent. In certain embodiments, N² is a modified cytosine. In certain embodiments, N² is 5-methylcytosine. In certain embodiments, N² is an unmodified cytosine. In certain embodiments, N² is an abasic sugar moiety. In certain embodiments, N² is a terminal group. In certain embodiments, N² is absent. In certain embodiments, N³ is a modified thymine. In certain embodiments, N³ is an unmodified thymine. In certain embodiments, N³ is an abasic sugar moiety. In certain embodiments, N³ is a terminal
 30 group. In certain embodiments, N³ is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N² is a modified cytosine. In certain embodiments, N¹ is an adenine nucleobase and N² is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N² is a terminal group. In certain
 35 embodiments, N¹ is an adenine nucleobase and N² is absent. In certain embodiments, N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a modified adenine and N² is 5-methylcytosine. In certain embodiments, N¹ is a modified adenine and N² is an abasic sugar moiety. In certain
 embodiments, N¹ is a modified adenine and N² is a terminal group. In certain embodiments, N¹ is a modified adenine and N² is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an

abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N² is a modified cytosine. In certain embodiments, N¹ is a hypoxanthine and N² is 5-methylcytosine. In certain embodiments, N¹ is a hypoxanthine and N² is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N² is a terminal group. In certain embodiments, N¹ is a hypoxanthine and N² is absent. In certain embodiments, N¹ is an abasic sugar moiety and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N² is absent. In certain embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is an adenine nucleobase and N³ is a thymine nucleobase. In certain embodiments, N¹ is an adenine nucleobase and N³ is a modified thymine. In certain embodiments, N¹ is an adenine nucleobase and N³ is an abasic sugar moiety. In certain embodiments, N¹ is an adenine nucleobase and N³ is a terminal group. In certain embodiments, N¹ is an adenine nucleobase and N³ is absent. In certain embodiments, N¹ is a modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a modified adenine and N³ is an unmodified thymine. In certain embodiments, N¹ is a modified adenine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a modified adenine and N³ is a terminal group. In certain embodiments, N¹ is a modified adenine and N³ is absent. In certain embodiments, N¹ is a hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a hypoxanthine and N³ is an unmodified thymine. In certain embodiments, N¹ is a hypoxanthine and N³ is an abasic sugar moiety. In certain embodiments, N¹ is a hypoxanthine and N³ is a terminal group. In certain embodiments, N¹ is a hypoxanthine and N³ is absent. In certain embodiments, N¹ is an abasic sugar moiety and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent. In certain embodiments, N¹ is absent and N³ is absent.

VIII. Certain Compositions

1. Compound No. 1601260

Compound No. 1601260 is characterized as a 5-10-5 MOE gapmer of linked nucleosides having a nucleobase sequence (from 5' to 3') of ACAGATATTTTGTCTGCC (SEQ ID NO: 3318), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 1 to 2, 2 to 3, 3 to 4, 4 to 5, 5 to 6, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 16 to 17, 17 to 18, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, wherein the internucleoside linkages between nucleosides 6 to 7, 7 to 8, 8 to 9, and 9 to 10 are mesyl phosphoramidate internucleoside linkages, and wherein each cytosine is a 5-methylcytosine.

Compound No. 1601260 is represented by the following chemical notation:

A_{es}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{dz}T_{ds}T_{ds}T_{ds}G_{ds}T_{ds}T_{ds}^mC_{es}T_{es}G_{es}^mC_{es}^mC_e (SEQ ID NO: 3335), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

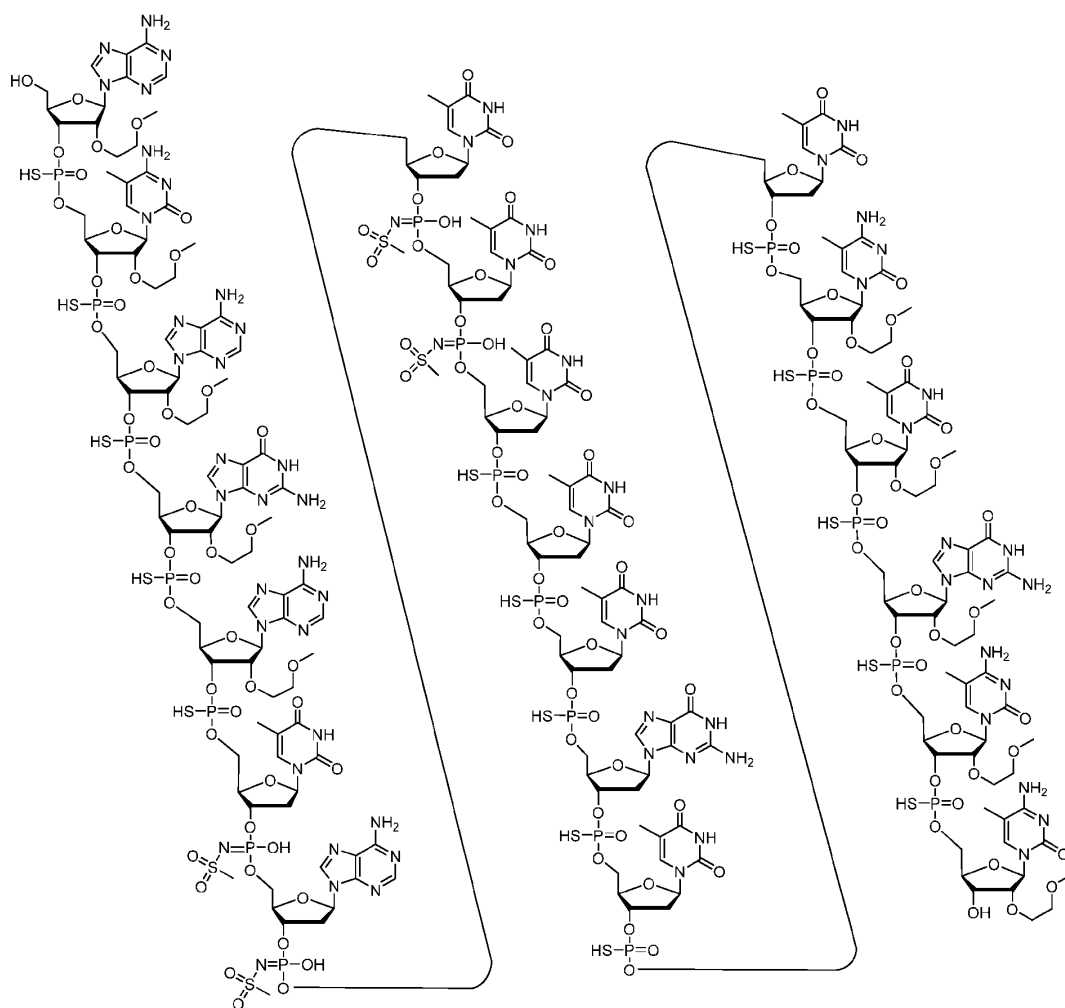
e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

5 s = a phosphorothioate internucleoside linkage, and

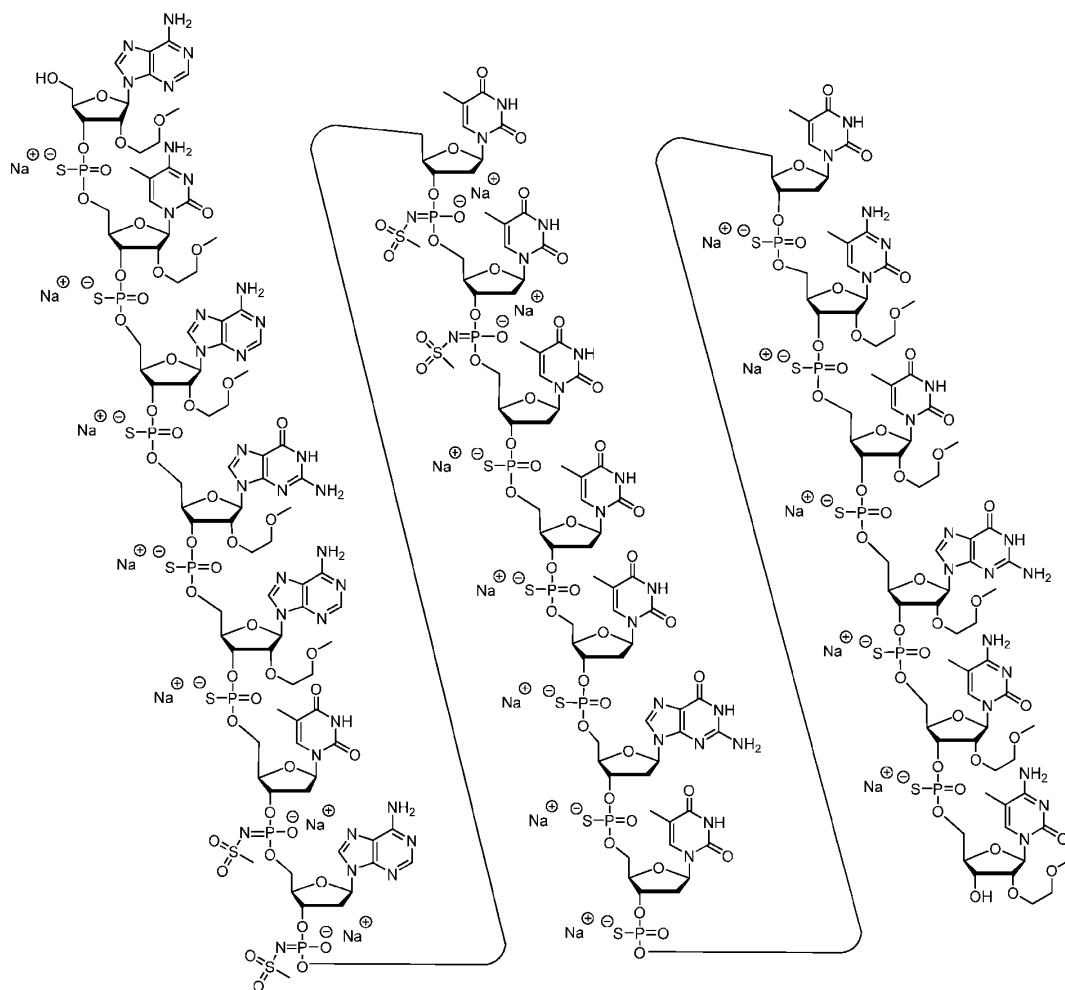
z = a mesyl phosphoramidate internucleoside linkage; and the compound does not include a conjugate group or a terminal group.

Compound No. 1601260 is represented by the following chemical structure:



10 (SEQ ID NO: 3335) (Structure 1), or a pharmaceutically acceptable salt thereof. The pharmaceutically acceptable salt of Compound No. 1601260 comprises one or more cations selected from sodium, potassium, calcium, and magnesium.

The sodium salt of Compound No. 1601260 is represented by the following chemical structure:



(SEQ ID NO: 3335) (Structure 2).

5 2. Compound No. 1616039

Compound No. 1616039 is characterized as a 5'-10-5 MOE gapmer of linked nucleosides having a nucleobase sequence (from 5' to 3') of ACGACATTTTCTTGCCTCTT (SEQ ID NO: 3319), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 1 to 2, 2 to 3, 5 to 6, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 14 to 15, 15 to 16, 16 to 17, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, wherein the internucleoside linkages between nucleosides 3 to 4, 4 to 5, and 17 to 18 are phosphodiester internucleoside linkages, wherein the internucleoside linkages between nucleosides 6 to 7 and 13 to 14 are mesyl phosphoramidate internucleoside linkages, and wherein each cytosine is a 5-methylcytosine.

Compound No. 1616039 is represented by the following chemical notation:

15 A_{es}^mC_{es}G_{eo}A_{eo}^mC_{es}A_{dz}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{ds}G_{ds}^mC_{ds}^mC_{es}T_{eo}^mC_{es}T_{es}T_e (SEQ ID NO: 3336), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

5 e = a 2'-MOE sugar moiety,

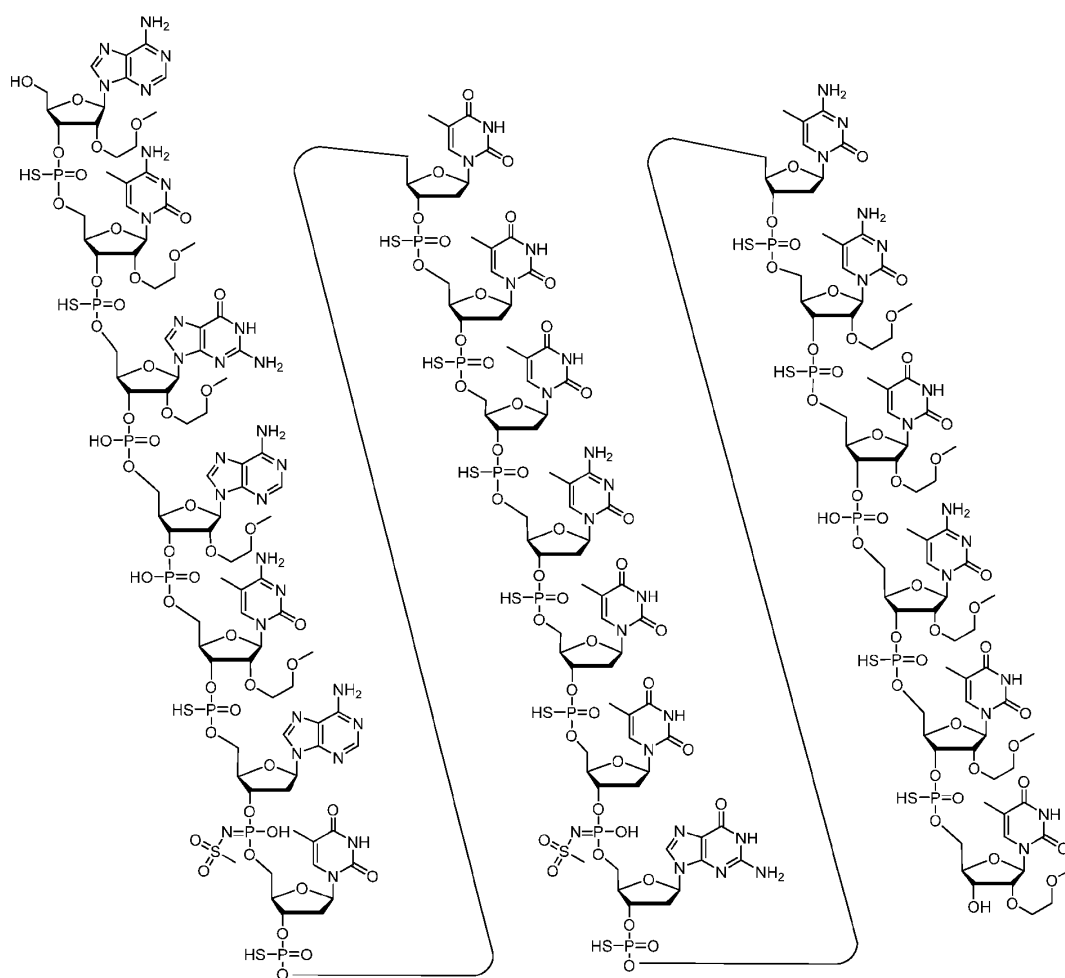
d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage,

z = a mesyl phosphoramidate internucleoside linkage, and

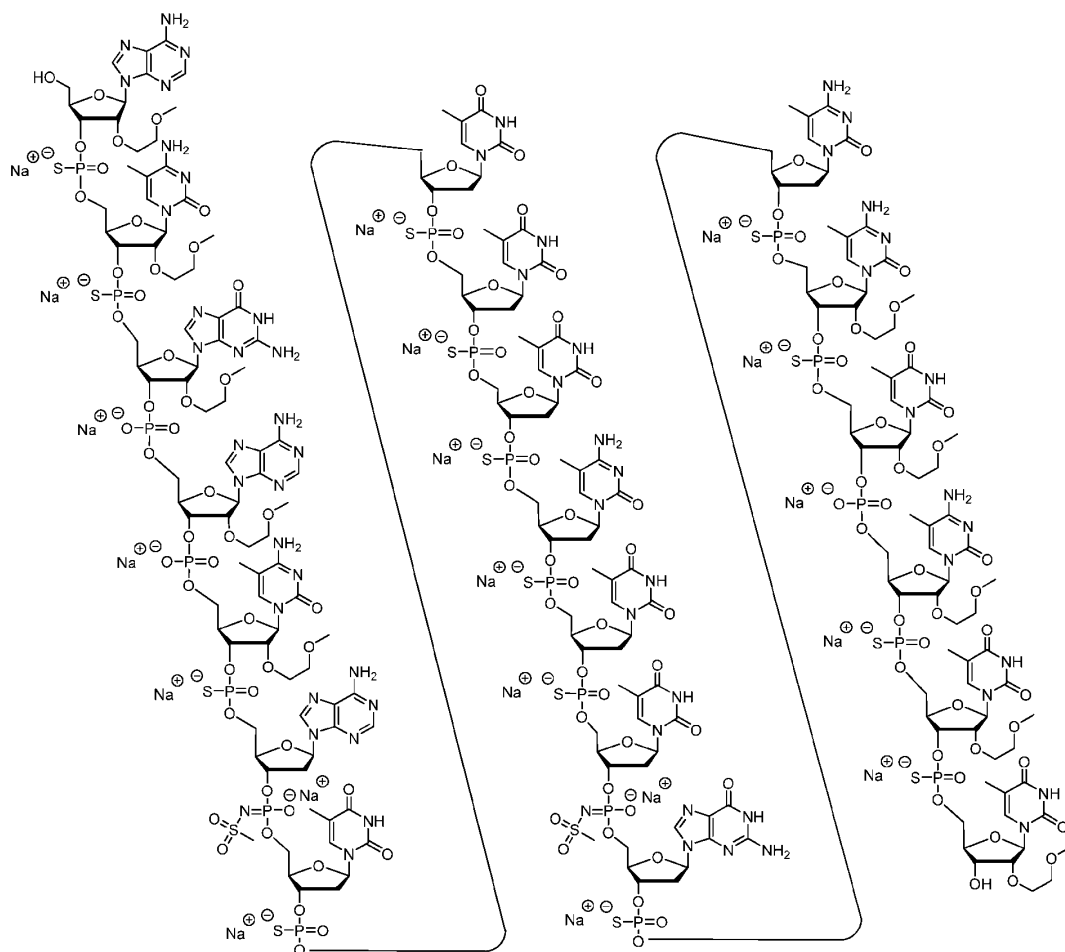
10 o = a phosphodiester internucleoside linkage; and the compound does not include a conjugate group or a terminal group.

Compound No. 1616039 is represented by the following chemical structure:



(SEQ ID NO: 3336) (Structure 3), or a pharmaceutically acceptable salt. The pharmaceutically acceptable salt of Compound No. 1616039 comprises one or more cations selected from sodium, potassium, calcium, and magnesium.

The sodium salt of Compound No. 1616039 is represented by the following chemical structure:



(SEQ ID NO: 3336) (Structure 4).

3. Compound No. 1616357

Compound No. 1616357 is characterized as a 5-10-5 MOE gapmer of linked nucleosides having a nucleobase sequence (from 5' to 3') of ACAGATATTTTGTCTGCC (SEQ ID NO: 3318), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 1 to 2, 2 to 3, 3 to 4, 4 to 5, 5 to 6, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 14 to 15, 15 to 16, 16 to 17, 17 to 18, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, wherein the internucleoside linkages between nucleosides 6 to 7, 7 to 8, 12 to 13, and 13 to 14 are mesyl phosphoramidate internucleoside linkages, and wherein each cytosine is a 5-methylcytosine.

Compound No. 1616357 is represented by the following chemical notation:

$A_{es}^m C_{es} A_{es} G_{es} A_{es} T_{dz} A_{dz} T_{ds} T_{ds} T_{ds} T_{ds} T_{dz} G_{dz} T_{ds} T_{ds}^m C_{es} T_{es} G_{es}^m C_{es}^m C_e$ (SEQ ID NO: 3337), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase.

G = a guanine nucleobase,

T = a thymine nucleobase,

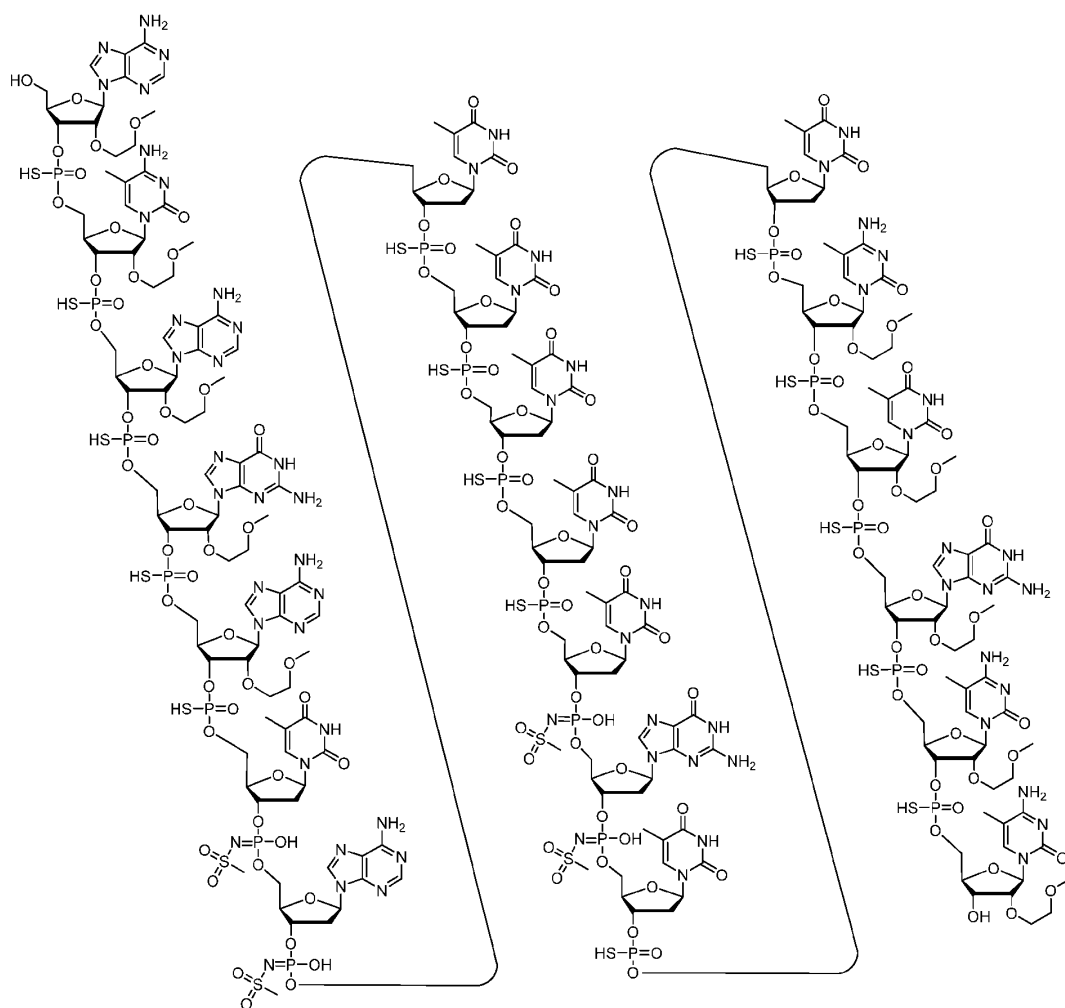
e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

5 s = a phosphorothioate internucleoside linkage, and

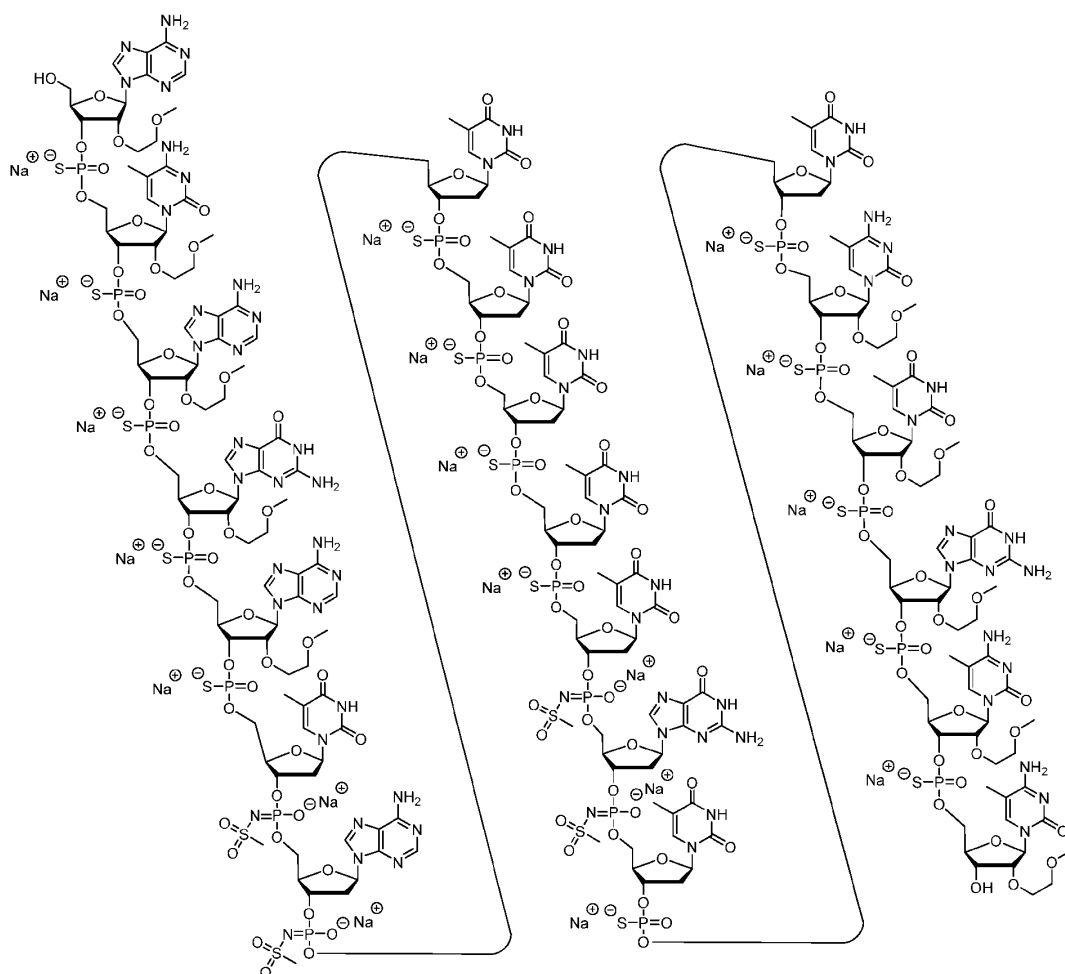
z = a mesyl phosphoramidate internucleoside linkage; and the compound does not include a conjugate group or a terminal group.

Compound No. 1616357 is represented by the following chemical structure:



10 (SEQ ID NO: 3337) (Structure 5), or a pharmaceutically acceptable salt thereof. The pharmaceutically acceptable salt of Compound No. 1616357 comprises one or more cations selected from sodium, potassium, calcium, and magnesium.

The sodium salt of Compound No. 1616357 is represented by the following chemical structure:



(SEQ ID NO: 3337) (Structure 6).

5 4. Compound No. 1620605

Compound No. 1620605 is characterized as a 6-10-4 MOE gapmer of linked nucleosides having a nucleobase sequence (from 5' to 3') of ATCACGACATTTTCTTGCCT (SEQ ID NO: 3328), wherein each of nucleosides 1-6 and 17-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 7-16 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 1 to 2, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 16 to 17, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 5 to 6, 6 to 7, and 17 to 18 are phosphodiester internucleoside linkages, and wherein each cytosine is a 5-methylcytosine.

Compound No. 1620605 is represented by the following chemical notation:

$A_{es}T_{co}^mC_{co}A_{co}^mC_{co}G_{co}A_{ds}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}T_{ds}C_{ds}T_{ds}T_{ds}G_{co}^mC_{es}^mC_{es}T_c$ (SEQ ID NO: 3338), wherein:

15 A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase.

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

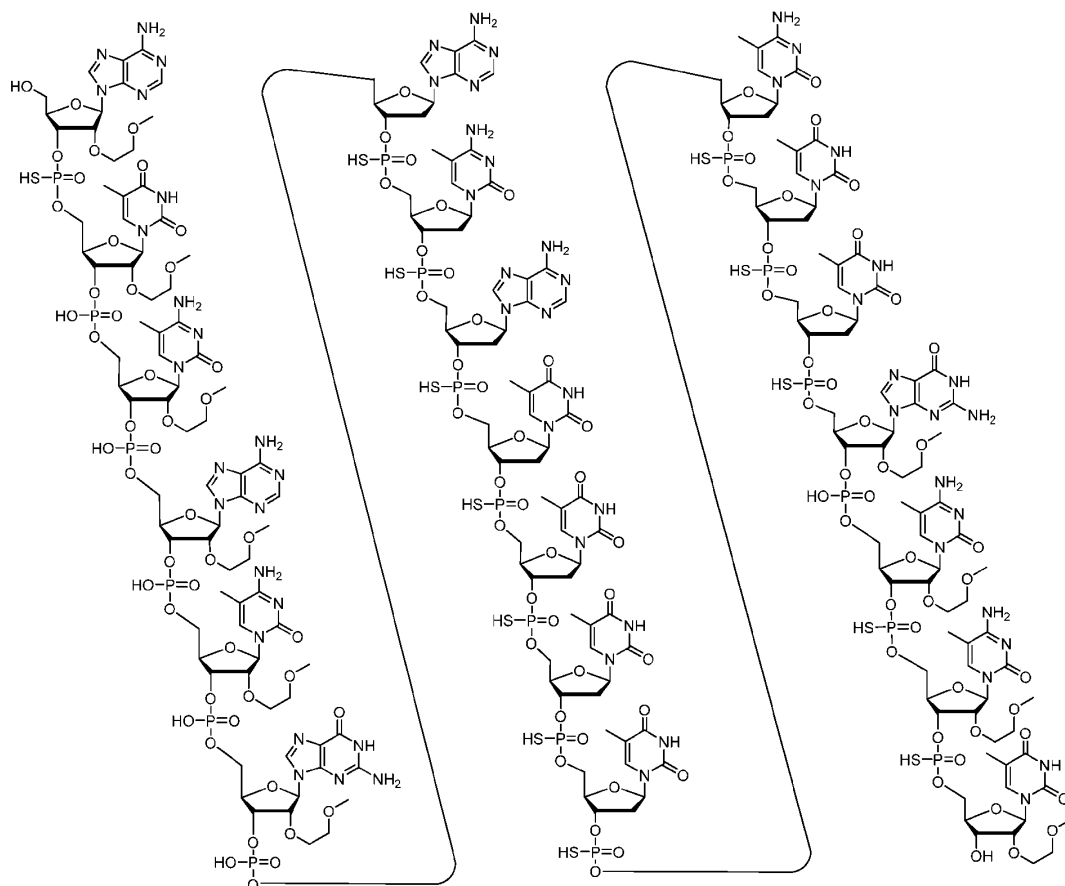
5 d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and the compound does not include a conjugate group or a

terminal group.

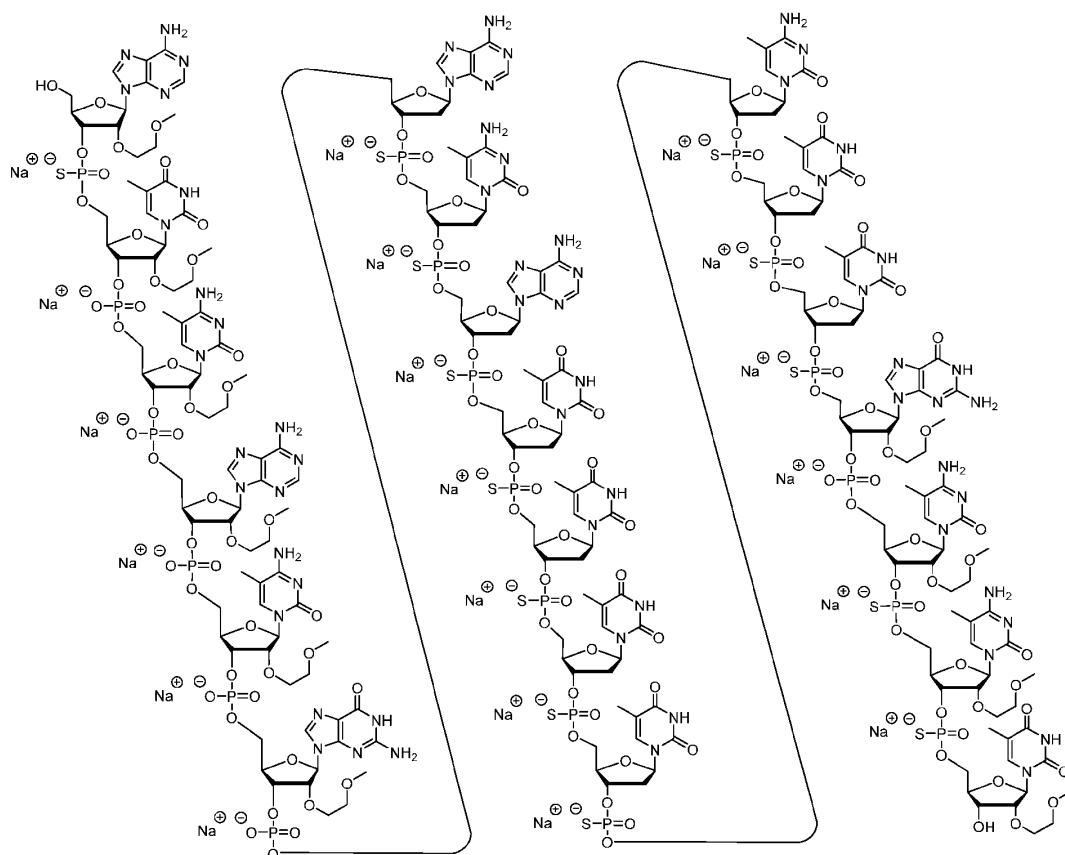
Compound No. 1620605 is represented by the following chemical structure:



10

(SEQ ID NO: 3338) (Structure 7), or a pharmaceutically acceptable salt thereof. The pharmaceutically acceptable salt of Compound No. 1620605 comprises one or more cations selected from sodium, potassium, calcium, and magnesium.

The sodium salt of Compound No. 1620605 is represented by the following chemical structure:



(SEQ ID NO: 3338) (Structure 8).

5 IX. Certain Comparator Compositions

In certain embodiments, compound 827599 is a comparator compound and is previously described in WO 2019/164562. Compound 827599 consists of the nucleobase sequence (from 5' to 3'): ACAGATATTTTGTCTGCC, designated herein as SEQ ID NO: 3318. The sugar motif for Compound No. 827599 is (from 5' to 3'): cccccccccccccccc; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "c" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 827599 is (from 5' to 3'): sossssssssssooss; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 827599 is a 5-methylcytosine.

In certain embodiments, compound 763364 is a comparator compound and is previously described in WO 2019/164562. Compound 763364 consists of the nucleobase sequence (from 5' to 3'): ACGACATTTTCTTGCTCTT, designated herein as SEQ ID NO: 3319. The sugar motif for Compound No. 763364 is (from 5' to 3'): eeeeeccccccccccc; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 763364 is (from 5' to 3'):

sooooooooooooo; wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 763364 is a 5-methylcytosine.

In certain embodiments, compounds described herein are superior relative to compounds described in WO2019/164562, because they demonstrate one or more improved properties, such as duration of action and potency.

5 For example, Compound No. 1601260, Compound No. 1616357, and Compound No. 1616039 each demonstrated a longer duration of action *in vivo* as compared to Compound No. 827599 in the assay shown in Example 13. In particular, Compound No. 1601260, Compound No. 1616357, and Compound No. 1616039 achieved a 48%, 58%, and 60% reduction of human SNCA RNA, respectively, at day 224 post-dose. In comparison, Compound No. 827599 achieved a 0% reduction of human SNCA RNA at day 224 post-dose. Therefore, each of Compound No.
10 1601260, Compound No. 1616357, and Compound No. 1616039 exhibited a longer duration of action compared to Compound No. 827599 in this assay.

For example, Compound No. 1601260, Compound No. 1616357, and Compound No. 1616039 each demonstrated improved potency *in vivo* compared to Compound No. 827599 (see Example 14) and to Compound No. 763364 (see Example 22). In particular, Compound No. 1601260, Compound No. 1616357, and Compound No.
15 1616039 achieved an ED₅₀ in the cortical brain tissue of 46μg, 29μg, and 23μg, respectively. In comparison, Compound No. 827599 achieved an ED₅₀ in the cortical brain tissue of 122μg and Compound No. 763374 achieved an ED₅₀ in the cortical brain tissue of 63μg. As such, each of Compound No. 1601260, Compound No. 1616357, and Compound No. 1616039 was more potent than Compound No. 827599 and Compound No. 763364 in these assays.

X. Certain Hotspot Regions

20 1. Nucleobases 16,692-16,716 of SEQ ID NO: 1 or nucleobases 18,758-18,782 of SEQ ID NO: 2

In certain embodiments, nucleobases 16,692-16,716 of SEQ ID NO: 1 or nucleobases 18,758-18,782 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 16,692-16,716 of SEQ ID NO: 1 or within nucleobases 18,758-18,782 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified
25 oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

30 In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkkee, kkkkkkkkkkkkkkeee, ekkkkkkkkkkkkkeeee, kkkkkkkkkkkkkkee, or
35 kkkkkkkkkkkkeeee; wherein “k” represents a cEt sugar moiety, “e” represents a 2'-MOE sugar moiety, and “d” represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooooooos, soooooooooos, soooooooooos,

soooooooooos, soooooooooos, soooooooooos, or soooooooooos; wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 78, 2564, 2697, 2747, 2789, 2936, 3063, 3081, 3142, 3189, and 3271 are complementary to an equal length portion within nucleobases 16,692-16,716 of SEQ ID NO: 1 or within nucleobases 18,758-18,782 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1483635, 1484499, 1485433, 1486327, 1486437, 1486657, 1535220, 1535277, 1535335, 1535391, 1535466, 1535496, 1535524, 1535578, and 1535629 are complementary to an equal length portion within nucleobases 16,692-16,716 of SEQ ID NO: 1 or within nucleobases 18,758-18,782 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 16,692-16,716 of SEQ ID NO: 1 or within nucleobases 18,758-18,782 of SEQ ID NO: 2 achieve at least 72% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 16,692-16,716 of SEQ ID NO: 1 or within nucleobases 18,758-18,782 of SEQ ID NO: 2 achieve an average of 88.9% reduction of SNCA mRNA in the standard *in vitro* assay.

2. Nucleobases 18,568-18,593 of SEQ ID NO: 1 or nucleobases 20,634-20,659 of SEQ ID NO: 2

In certain embodiments, nucleobases 18,568-18,593 of SEQ ID NO: 1 or nucleobases 20,634-20,659 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 18,568-18,593 of SEQ ID NO: 1 or within nucleobases 20,634-20,659 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkee, kkkkkkkkkkkkkeee, kkkkkkkkkkkkeeee, or kkkkkkkkkkkkeeee; wherein “k” represents a cEt sugar moiety, “e” represents a 2'-MOE sugar moiety, and “d” represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, or soooooooooos; wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 206, 231, 270, 316, 2486, 2558, 3041, 3076, 3137, 3184, and 3266 are complementary to an equal length portion within nucleobases 18,568-18,593 of SEQ ID NO: 1 or within nucleobases 20,634-20,659 of SEQ ID NO: 2.

5 The nucleobase sequences of Compound Nos: 1482920, 1484352, 1534261, 1534329, 1534428, 1534460, 1535214, 1535272, 1535330, 1535386, 1535439, 1535460, 1535518, and 1535573 are complementary to an equal length portion within nucleobases 18,568-18,593 of SEQ ID NO: 1 or within nucleobases 20,634-20,659 of SEQ ID NO: 2.

10 In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,568-18,593 of SEQ ID NO: 1 or within nucleobases 20,634-20,659 of SEQ ID NO: 2 achieve at least 73% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,568-18,593 of SEQ ID NO: 1 or within nucleobases 20,634-20,659 of SEQ ID NO: 2 achieve an average of 88.1% reduction of SNCA mRNA in the standard *in vitro* assay.

3. Nucleobases 18,621-18,649 of SEQ ID NO: 1 or nucleobases 20,687-20,715 of SEQ ID NO: 2

15 In certain embodiments, nucleobases 18,621-18,649 of SEQ ID NO: 1 or nucleobases 20,687-20,715 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 18,621-18,649 of SEQ ID NO: 1 or within nucleobases 20,687-20,715 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

20 In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkcc, kkkkkkkkkkkkkccc, ckkkkkkkkkkkkcccc, kkkkkkkkkkkkkccc, or kkkkkkkkkkkkkeeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

30 In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssssos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, or soossssssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 64, 128, 289, 921, 2744, 2853, 2922, 3031, 3057, 3099, 3123, 3132, 3160, 3207, 3231, 3289, and 3313 are complementary to an equal length portion within nucleobases 18,621-18,649 of SEQ ID NO: 1 or within nucleobases 20,687-20,715 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1485236, 1485314, 1485897, 1486071, 1486591, 1533975, 1534327, 1535209, 1535240, 1535266, 1535297, 1535315, 1535324, 1535355, 1535381, 1535411, 1535437, 1535455, 1535487, 1535513, 1535543, 1535568, 1535598, and 1535628 are complementary to an equal length portion within nucleobases 18,621-18,649 of SEQ ID NO: 1 or within nucleobases 20,687-20,715 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,621-18,649 of SEQ ID NO: 1 or within nucleobases 20,687-20,715 of SEQ ID NO: 2 achieve at least 61% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,621-18,649 of SEQ ID NO: 1 or within nucleobases 20,687-20,715 of SEQ ID NO: 2 achieve an average of 85.7% reduction of SNCA mRNA in the standard *in vitro* assay.

4. Nucleobases 18,721-18,752 of SEO ID NO: 1 or nucleobases 20,787-20,818 of SEO ID NO: 2

In certain embodiments, nucleobases 18,721-18,752 of SEQ ID NO: 1 or nucleobases 20,787-20,818 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 18,721-18,752 of SEQ ID NO: 1 or within nucleobases 20,787-20,818 of SEQ ID NO: 2.

2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkee, kkkdddddskkee, ekkdddddskkee, kkkdddddskkee, or kkkdddddskkee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, or soossssssssssss; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 227, 427, 545, 1214, 1279, 1385, 1401, 1476, 1616, 3048, 3115, 3176, and 3305 are complementary to an equal length portion within nucleobases 18,721-18,752 of SEQ ID NO: 1 or within nucleobases 20,787-20,818 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1482396, 1483241, 1485037, 1485579, 1486302, 1486305, 1533429, 1534037, 1534406, 1535257, 1535316, 1535372, 1535428, 1535446, 1535504, 1535615, and 1535621 are complementary to an equal length portion within nucleobases 18,721-18,752 of SEQ ID NO: 1 or within nucleobases 20,787-20,818 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,721-18,752 of SEQ ID NO: 1 or within nucleobases 20,787-20,818 of SEQ ID NO: 2 achieve at least

66% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 18,721-18,752 of SEQ ID NO: 1 or within nucleobases 20,787-20,818 of SEQ ID NO: 2 achieve an average of 85.6% reduction of SNCA mRNA in the standard *in vitro* assay.

5 **5. Nucleobases 19,423-19,443 of SEQ ID NO: 1 or nucleobases 21,489-21,509 of SEQ ID NO: 2**

In certain embodiments, nucleobases 19,423-19,443 of SEQ ID NO: 1 or nucleobases 21,489-21,509 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 19,423-19,443 of SEQ ID NO: 1 or within nucleobases 21,489-21,509 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkkee, kkkkkkkkkkkkkkee, kkkkkkkkkkkkkkee, or kkkkkkkkkkkkkkee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, or soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 203, 285, 1974, 2044, 2949, 3021, 3090, 3151, 3198, and 3280 are complementary to an equal length portion within nucleobases 19,423-19,443 of SEQ ID NO: 1 or within nucleobases 21,489-21,509 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484583, 1485328, 1485484, 1534314, 1534320, 1535215, 1535230, 1535287, 1535345, 1535401, 1535477, 1535533, and 1535588 are complementary to an equal length portion within nucleobases 19,423-19,443 of SEQ ID NO: 1 or within nucleobases 21,489-21,509 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 19,423-19,443 of SEQ ID NO: 1 or within nucleobases 21,489-21,509 of SEQ ID NO: 2 achieve at least 79% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 19,423-19,443 of SEQ ID NO: 1 or within nucleobases 21,489-21,509 of SEQ ID NO: 2 achieve an average of 88.6% reduction of SNCA mRNA in the standard *in vitro* assay.

6. Nucleobases 19,555-19,575 of SEQ ID NO: 1 or nucleobases 21,621-21,641 of SEQ ID NO: 2

In certain embodiments, nucleobases 19,555-19,575 of SEQ ID NO: 1 or nucleobases 21,621-21,641 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 19,555-19,575 of SEQ ID NO: 1 or within nucleobases 21,621-21,641 of SEQ ID NO:

2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkkee, kkkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, or soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 205, 2594, 2686, 3028, 3097, 3158, 3205, and 3287 are complementary to an equal length portion within nucleobases 19,555-19,575 of SEQ ID NO: 1 or within nucleobases 21,621-21,641 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1485166, 1486157, 1534324, 1535238, 1535292, 1535295, 1535352, 1535409, 1535484, 1535540, and 1535596 are complementary to an equal length portion within nucleobases 19,555-19,575 of SEQ ID NO: 1 or within nucleobases 21,621-21,641 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 19,555-19,575 of SEQ ID NO: 1 or within nucleobases 21,621-21,641 of SEQ ID NO: 2 achieve at least 77% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 19,555-19,575 of SEQ ID NO: 1 or within nucleobases 21,621-21,641 of SEQ ID NO: 2 achieve an average of 89.5% reduction of SNCA mRNA in the standard *in vitro* assay.

7. Nucleobases 21,457-21,501 of SEQ ID NO: 1 or nucleobases 23,523-23,567 of SEQ ID NO: 2

In certain embodiments, nucleobases 21,457-21,501 of SEQ ID NO: 1 or nucleobases 23,523-23,567 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 21,457-21,501 of SEQ ID NO: 1 or within nucleobases 23,523-23,567 of SEQ ID NO:

2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified

oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkkee. kkkkkkkkkkkkkkee. ekkkkkkkkkkkkkeee. kkkkkkkkkkkkkkee, or kkkkkkkkkkkkkkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssssos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soosssssssssssss, or soooooossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 214, 247, 865, 1887, 1948, 3067, 3085, 3146, 3193, and 3275 are complementary to an equal length portion within nucleobases 21,457-21,501 of SEQ ID NO: 1 or within nucleobases 23,523-23,567 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1483319, 1483650, 1483923, 1485260, 1534362, 1535224, 1535282, 1535339, 1535396, 1535470, 1535528, 1535563, 1535583, and 1535631 are complementary to an equal length portion within nucleobases 21,457-21,501 of SEQ ID NO: 1 or within nucleobases 23,523-23,567 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 21,457-21,501 of SEQ ID NO: 1 or within nucleobases 23,523-23,567 of SEQ ID NO: 2 achieve at least 73% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 21,457-21,501 of SEQ ID NO: 1 or within nucleobases 23,523-23,567 of SEQ ID NO: 2 achieve an average of 86.6% reduction of SNCA mRNA in the standard *in vitro* assay.

8. Nucleobases 22,008-22,030 of SEQ ID NO: 1 or nucleobases 24,074-24,096 of SEQ ID NO: 2

In certain embodiments, nucleobases 22,008-22,030 of SEQ ID NO: 1 or nucleobases 24,074-24,096 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 22,008-22,030 of SEQ ID NO: 1 or within nucleobases 24,074-24,096 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain

embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkee, kkkkkkkkkkkkkeee, ekkkkkkkkkkkkeeee, kkkkkkkkkkkkkeee, or kkkkkkkkkkkkkeeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, soooooooooos, or soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 167, 208, 248, 304, 1930, 3054, 3120, 3129, 3228, and 3310 are complementary to an equal length portion within nucleobases 22,008-22,030 of SEQ ID NO: 1 or within nucleobases 24,074-24,096 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1483819, 1484024, 1486466, 1534334, 1534403, 1535206, 1535263, 1535321, 1535377, 1535434, 1535452, 1535510, 1535565, and 1535625 are complementary to an equal length portion within nucleobases 22,008-22,030 of SEQ ID NO: 1 or within nucleobases 24,074-24,096 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,008-22,030 of SEQ ID NO: 1 or within nucleobases 24,074-24,096 of SEQ ID NO: 2 achieve at least 75% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,008-22,030 of SEQ ID NO: 1 or within nucleobases 24,074-24,096 of SEQ ID NO: 2 achieve an average of 89% reduction of SNCA mRNA in the standard *in vitro* assay.

9. Nucleobases 22,507-22,529 of SEQ ID NO: 1 or nucleobases 24,573-24,595 of SEQ ID NO: 2

In certain embodiments, nucleobases 22,507-22,529 of SEQ ID NO: 1 or nucleobases 24,573-24,595 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 22,507-22,529 of SEQ ID NO: 1 or within nucleobases 24,573-24,595 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-

10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkkee, kkkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, or soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 196, 1814, 1909, 3042, 3109, 3170, 3217, and 3299 are complementary to an equal length portion within nucleobases 22,507-22,529 of SEQ ID NO: 1 or within nucleobases 24,573-24,595 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484851, 1485878, 1534284, 1535251, 1535308, 1535365, 1535422, 1535440, 1535498, 1535553, and 1535609 are complementary to an equal length portion within nucleobases 22,507-22,529 of SEQ ID NO: 1 or within nucleobases 24,573-24,595 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,507-22,529 of SEQ ID NO: 1 or within nucleobases 24,573-24,595 of SEQ ID NO: 2 achieve at least 78% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,507-22,529 of SEQ ID NO: 1 or within nucleobases 24,573-24,595 of SEQ ID NO: 2 achieve an average of 89.4% reduction of SNCA mRNA in the standard *in vitro* assay.

10. Nucleobases 22,614-22,637 of SEQ ID NO: 1 or nucleobases 24,680-24,703 of SEQ ID NO: 2

In certain embodiments, nucleobases 22,614-22,637 of SEQ ID NO: 1 or nucleobases 24,680-24,703 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 22,614-22,637 of SEQ ID NO: 1 or within nucleobases 24,680-24,703 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkkee, kkkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssssos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, or soooooossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 171, 207, 245, 489, 2390, 3053, 3119, 3128, 3227, and 3309 are complementary to an equal length portion within nucleobases 22,614-22,637 of SEQ ID NO: 1 or within nucleobases 24,680-24,703 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1482571, 1486455, 1533179, 1534179, 1534332, 1535205, 1535262, 1535320, 1535376, 1535433, 1535451, 1535509, and 1535564 are complementary to an equal length portion within nucleobases 22,614-22,637 of SEQ ID NO: 1 or within nucleobases 24,680-24,703 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,614-22,637 of SEQ ID NO: 1 or within nucleobases 24,680-24,703 of SEQ ID NO: 2 achieve at least 57% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 22,614-22,637 of SEQ ID NO: 1 or within nucleobases 24,680-24,703 of SEQ ID NO: 2 achieve an average of 87.2% reduction of SNCA mRNA in the standard *in vitro* assay.

11. Nucleobases 25,049-25,090 of SEQ ID NO: 1 or nucleobases 27,115-27,156 of SEQ ID NO: 2

In certain embodiments, nucleobases 25,049-25,090 of SEQ ID NO: 1 or nucleobases 27,115-27,156 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 25,049-25,090 of SEQ ID NO: 1 or within nucleobases 27,115-27,156 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkkee, kkkkkkkkkkkkkkee, ekkkkkkkkkkkkkeee, kkkkkkkkkkkkkkee, or kkkkkkkkkkkkkkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssssos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, or soooooossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 24, 133, 199, 228, 230, 276, 314, 946, 2759, 2818, 2873, 3069, 3087, 3148, 3195, and 3277 are complementary to an equal length portion within nucleobases 25,049-25,090 of SEQ ID NO: 1 or within nucleobases 27,115-27,156 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484502, 1484512, 1484515, 1485351, 1485506, 1485716, 1534281, 1534299, 1534409, 1534422, 1534454, 1535227, 1535284, 1535342, 1535398, 1535472, 1535530, 1535585, 1535592, and 1535633 are complementary to an equal length portion within nucleobases 25,049-25,090 of SEQ ID NO: 1 or within nucleobases 27,115-27,156 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 25,049-25,090 of SEQ ID NO: 1 or within nucleobases 27,115-27,156 of SEQ ID NO: 2 achieve at least 71% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 25,049-25,090 of SEQ ID NO: 1 or within nucleobases 27,115-27,156 of SEQ ID NO: 2 achieve an average of 85.5% reduction of SNCA mRNA in the standard *in vitro* assay.

12. Nucleobases 26,367-26,388 of SEQ ID NO: 1 or nucleobases 28,433-28,454 of SEQ ID NO: 2

In certain embodiments, nucleobases 26,367-26,388 of SEQ ID NO: 1 or nucleobases 28,433-28,454 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 26,367-26,388 of SEQ ID NO: 1 or within nucleobases 28,433-28,454 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkcc, kkkkkkkkkkkkkccc, ckkkkkkkkkkkkcccc, kkkkkkkkkkkkkccc, or kkkkkkkkkkkkkceee; wherein "k" represents a cEt sugar moiety, "c" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssssos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, soossssssssssoos, or soooooossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 168, 193, 236, 313, 2446, 3049, 3116, 3177, 3224, and 3306 are complementary to an equal length portion within nucleobases 26,367-26,388 of SEQ ID NO: 1 or within nucleobases 28,433-28,454 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1485739, 1486339, 1534264, 1534442, 1534444, 1535258, 1535317, 1535373, 1535429, 1535447, 1535505, 1535560, 1535616, and 1535622 are complementary to an equal length portion within nucleobases 26,367-26,388 of SEQ ID NO: 1 or within nucleobases 28,433-28,454 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 26,367-26,388 of SEQ ID NO: 1 or within nucleobases 28,433-28,454 of SEQ ID NO: 2 achieve at least 76% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 26,367-26,388 of SEQ ID NO: 1 or within nucleobases 28,433-28,454 of SEQ ID NO: 2 achieve an average of 90.5% reduction of SNCA mRNA in the standard *in vitro* assay.

13. Nucleobases 26,508-26,531 of SEQ ID NO: 1 or nucleobases 28,574-28,597 of SEQ ID NO: 2

In certain embodiments, nucleobases 26,508-26,531 of SEQ ID NO: 1 or nucleobases 28,574-28,597 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 26,508-26,531 of SEQ ID NO: 1 or within nucleobases 28,574-28,597 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkddddd kkeee, kkkddddd kkeee, ekkddddd kkeeee, kkkddddd kkeee, or kkkddddd kkeeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssoos, soossssssoos, soossssssoos, soossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 210, 223, 272, 273, 274, 1026, 1143, 3020, 3089, 3150, 3197, and 3279 are complementary to an equal length portion within nucleobases 26,508-26,531 of SEQ ID NO: 1 or within nucleobases 28,574-28,597 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484579, 1485953, 1534266, 1534267, 1534268, 1534341, 1534391, 1535203, 1535229, 1535286, 1535344, 1535400, 1535476, 1535532, 1535587, and 1535636 are complementary to an equal length portion within nucleobases 26,508-26,531 of SEQ ID NO: 1 or within nucleobases 28,574-28,597 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 26,508-26,531 of SEQ ID NO: 1 or within nucleobases 28,574-28,597 of SEQ ID NO: 2 achieve at least 78% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 26,508-26,531 of SEQ ID NO: 1 or within nucleobases 28,574-28,597 of SEQ ID NO: 2 achieve an average of 89.3% reduction of SNCA mRNA in the standard *in vitro* assay.

14. Nucleobases 30,207-30,226 of SEQ ID NO: 1 or nucleobases 32,273-32,292 of SEQ ID NO: 2

In certain embodiments, nucleobases 30,207-30,226 of SEQ ID NO: 1 or nucleobases 32,273-32,292 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 30,207-30,226 of SEQ ID NO: 1 or within nucleobases 32,273-32,292 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkkee, kkkdddddskkeee, ekkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, or soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 287, 964, 1040, 1154, 3050, 3117, 3178, 3225, and 3307 are complementary to an equal length portion within nucleobases 30,207-30,226 of SEQ ID NO: 1 or within nucleobases 32,273-32,292 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1485060, 1485105, 1486348, 1534322, 1535260, 1535318, 1535374, 1535430, 1535448, 1535506, 1535561, 1535617, and 1535623 are complementary to an equal length portion within nucleobases 30,207-30,226 of SEQ ID NO: 1 or within nucleobases 32,273-32,292 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 30,207-30,226 of SEQ ID NO: 1 or within nucleobases 32,273-32,292 of SEQ ID NO: 2 achieve at least 81% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 30,207-30,226 of SEQ ID NO: 1 or within nucleobases 32,273-32,292 of SEQ ID NO: 2 achieve an average of 92.9% reduction of SNCA mRNA in the standard *in vitro* assay.

15. Nucleobases 31,412-31,438 of SEQ ID NO: 1 or nucleobases 33,478-33,504 of SEQ ID NO: 2

In certain embodiments, nucleobases 31,412-31,438 of SEQ ID NO: 1 or nucleobases 33,478-33,504 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 31,412-31,438 of SEQ ID NO: 1 or within nucleobases 33,478-33,504 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain
 10 modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers
 15 are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkkkkkkkkkkkkee, kkkkkkkkkkkkkkee, ekkkkkkkkkkkkkeee, kkkkkkkkkkkkkkee, or kkkkkkkkkkkkeeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate
 20 internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooooooos, soooooooooos, soooooooooos, soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 119, 980, 1085, 1166, 3051, 3118, 3127, 3226, and 3308 are
 25 complementary to an equal length portion within nucleobases 31,412-31,438 of SEQ ID NO: 1 or within nucleobases 33,478-33,504 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484891, 1485806, 1486424, 1486626, 1535204, 1535261, 1535319, 1535375, 1535432, 1535449, 1535508, 1535562, and 1535624 are complementary to an equal length portion
 30 within nucleobases 31,412-31,438 of SEQ ID NO: 1 or within nucleobases 33,478-33,504 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within
 35 nucleobases 31,412-31,438 of SEQ ID NO: 1 or within nucleobases 33,478-33,504 of SEQ ID NO: 2 achieve at least 79% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 31,412-31,438 of SEQ ID NO: 1 or within nucleobases 33,478-33,504 of SEQ ID NO: 2 achieve an average of 86.8% reduction of SNCA mRNA in the standard *in vitro* assay.

16. Nucleobases 33,027-33,057 of SEQ ID NO: 1 or nucleobases 35,093-35,123 of SEQ ID NO: 2

In certain embodiments, nucleobases 33,027-33,057 of SEQ ID NO: 1 or nucleobases 35,093-35,123 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 33,027-33,057 of SEQ ID NO: 1 or within nucleobases 35,093-35,123 of SEQ ID NO: 2

2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkee, kkkdddddskkeee, ekkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribsyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sooooooooooooo, soooooooooooooo, soooooooooooooo, soooooooooooooo, soooooooooooooo, soooooooooooooo, soooooooooooooo, or soooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 194, 277, 1113, 1185, 1309, 3024, 3093, 3154, 3201, and 3283 are complementary to an equal length portion within nucleobases 33,027-33,057 of SEQ ID NO: 1 or within nucleobases 35,093-35,123 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1484757, 1485131, 1486277, 1534265, 1534282, 1535233, 1535248, 1535290, 1535348, 1535404, 1535480, 1535536, 1535591, and 1535637 are complementary to an equal length portion within nucleobases 33,027-33,057 of SEQ ID NO: 1 or within nucleobases 35,093-35,123 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 33,027-33,057 of SEQ ID NO: 1 or within nucleobases 35,093-35,123 of SEQ ID NO: 2 achieve at least 66% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 33,027-33,057 of SEQ ID NO: 1 or within nucleobases 35,093-35,123 of SEQ ID NO: 2 achieve an average of 86.9% reduction of SNCA mRNA in the standard *in vitro* assay.

17. Nucleobases 48,460-48,489 of SEQ ID NO: 1 or nucleobases 50,526-50,555 of SEQ ID NO: 2

In certain embodiments, nucleobases 48,460-48,489 of SEQ ID NO: 1 or nucleobases 50,526-50,555 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to an equal length portion within nucleobases 48,460-48,489 of SEQ ID NO: 1 or within nucleobases 50,526-50,555 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 16 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 18 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are cEt gapmers. In certain

embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are mixed cEt/MOE gapmers.

In certain embodiments, the gapmers are 3-10-3 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 cEt gapmers. In certain embodiments, the gapmers are 4-10-3 cEt gapmers. In certain embodiments, the gapmers are 4-10-4 cEt gapmers. In certain embodiments, the gapmers are 5-10-5 cEt gapmers. In certain embodiments, the gapmers are 3-10-4 or 3-10-5 mixed cEt/MOE gapmers. In certain embodiments, the sugar motif for the mixed cEt/MOE gapmers is (from 5' to 3'): kkkdddddskkee, kkkdddddskkeee, kkkdddddskkeee, or kkkdddddskkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribosyl sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, soossssssssoos, or soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 310, 803, 919, 1582, 1674, 3032, 3032, 3100, 3161, 3208, 3290, and 3290 are complementary to an equal length portion within nucleobases 48,460-48,489 of SEQ ID NO: 1 or within nucleobases 50,526-50,555 of SEQ ID NO: 2.

The nucleobase sequences of Compound Nos: 1485242, 1485665, 1533161, 1533933, 1534424, 1535241, 1535298, 1535327, 1535356, 1535412, 1535488, 1535544, and 1535599 are complementary to an equal length portion within nucleobases 48,460-48,489 of SEQ ID NO: 1 or within nucleobases 50,526-50,555 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 48,460-48,489 of SEQ ID NO: 1 or within nucleobases 50,526-50,555 of SEQ ID NO: 2 achieve at least 70% reduction of SNCA mRNA in the standard *in vitro* assay. In certain embodiments, modified oligonucleotides complementary to an equal length portion within nucleobases 48,460-48,489 of SEQ ID NO: 1 or within nucleobases 50,526-50,555 of SEQ ID NO: 2 achieve an average of 89.2% reduction of SNCA mRNA in the standard *in vitro* assay.

Nonlimiting disclosure and incorporation by reference

Each of the literature and patent publications listed herein is incorporated by reference in its entirety.

While certain compounds, compositions and methods described herein have been described with specificity in accordance with certain embodiments, the following examples serve only to illustrate the compounds described herein and are not intended to limit the same. Each of the references, GenBank accession numbers, ENSEMBL identifiers, and the like recited in the present application is incorporated herein by reference in its entirety.

The sequence listing accompanying this filing identifies each nucleic acid sequence as either "RNA" or "DNA" as required; however, one of skill in the art will readily appreciate that designation of "RNA" or "DNA" to describe modified oligonucleotides is, in certain instances, arbitrary. For example, an oligonucleotide comprising a nucleoside comprising a 2'-OH sugar moiety and a thymine base could be described as a DNA having a modified sugar (2'-OH in place of one 2'-H of DNA) or as an RNA having a modified base (thymine (5-methyl uracil)) in place of an uracil of RNA); and certain nucleic acid compounds described herein comprise one or more nucleosides comprising modified

sugar moieties having 2'-substituent(s) that are neither OH nor H. One of skill in the art will readily appreciate that labeling such nucleic acid compounds "RNA" or "DNA" does not alter or limit the description of such nucleic acid compounds.

Herein, the description of compounds as having "the nucleobase sequence of" a SEQ ID NO. describes only the nucleobase sequence. Accordingly, absent additional description, such description of compounds by reference to a nucleobase sequence of a SEQ ID NO. does not limit sugar or internucleoside linkage modifications or presence or absence of additional substituents such as a conjugate group. Further, absent additional description, the nucleobases of a compound "having the nucleobase sequence of" a SEQ ID NO. include such compounds having modified forms of the identified nucleobases as described herein.

Herein, the description of compounds by chemical notation (subscripts and/or superscripts to indicate chemical modifications) without reference to a specific Compound No. include only each noted modification, but may include additional substituents, such as a conjugate group, unless otherwise indicated. For example, the chemical notation of "A_{es}T_{ko}^mC_{ez}G_{ds}C_d" indicates a compound wherein the first nucleoside comprises a 2'-MOE sugar moiety (indicated by the "e" subscript) and an unmodified adenine nucleobase linked to the second nucleoside via a phosphorothioate linkage (indicated by the "s" subscript); the second nucleoside comprises a cEt sugar moiety (indicated by the "k" subscript) and an unmodified thymine nucleobase linked to the third nucleoside via a phosphodiester linkage (indicated by the "o" subscript); the third nucleoside comprises a 2'-MOE sugar moiety and a 5-methyl modified cytosine nucleobase (indicated by the "m" superscript) linked to the fourth nucleoside via a mesyl phosphoramidate linkage (indicated by the "z" subscript); the fourth nucleoside comprises a 2'-β-D-deoxyribose sugar moiety (indicated by the "d" subscript) and an unmodified guanine nucleobase linked to the fifth nucleoside with a phosphorothioate linkage; and the fifth nucleoside comprises a 2'-β-D-deoxyribose sugar moiety and an unmodified cytosine nucleobase; and the compound may include additional substituents, such as a conjugate group.

Herein, where a specific compound (e.g., with reference to a Compound No.) is described (as in the examples) by chemical notation, each nucleobase, sugar, and internucleoside linkage of such specific compound is modified only as indicated. Accordingly, in the context of a description of a specific compound having a particular Compound No., "A_{es}T_{ko}^mC_{ez}G_{ds}C_d" indicates a compound wherein the first nucleoside comprises a 2'-MOE sugar moiety (indicated by the "e" subscript) and an unmodified adenine nucleobase linked to the second nucleoside via a phosphorothioate linkage (indicated by the "s" subscript); the second nucleoside comprises a cEt sugar moiety (indicated by the "k" subscript) and an unmodified thymine nucleobase linked to the third nucleoside via a phosphodiester linkage (indicated by the "o" subscript); the third nucleoside comprises a 2'-MOE sugar moiety and a 5-methyl modified cytosine nucleobase (indicated by the "m" superscript) linked to the fourth nucleoside via a mesylphosphoramidate linkage (indicated by the "z" subscript); the fourth nucleoside comprises a 2'-β-D-deoxyribose sugar moiety (indicated by the "d" subscript) and an unmodified guanine nucleobase linked to the fifth nucleoside with a phosphorothioate linkage; and the fifth nucleoside comprises a 2'-β-D-deoxyribose sugar moiety and an unmodified cytosine nucleobase; and the compound does not include additional substituents.

Herein, sugar, internucleoside linkage, and nucleobase modifications may be indicated within a nucleotide or nucleobase sequence (e.g., by superscript or subscript, as shown above) or may be indicated in text accompanying a sequence (e.g., in separate text that appears within or above or below a table of compounds).

Where a specific compound is described herein by way of a drawn chemical structure, each nucleobase, sugar, and internucleoside linkage of such a specific compound includes only the modifications indicated in the drawn chemical structure. One of skill will appreciate, however, that drawn compounds may exist in equilibrium between tautomeric forms and/or as salts in equilibrium with protonated or ionic forms. Drawn structures are intended to capture all such forms of such compounds.

While effort has been made to accurately describe compounds in the accompanying sequence listing, should there be any discrepancies between a description in this specification and in the accompanying sequence listing, the description in the specification and not in the sequence listing is the accurate description.

The compounds described herein include variations in which one or more atoms are replaced with a non-radioactive isotope or radioactive isotope of the indicated element. For example, compounds herein that comprise hydrogen atoms encompass all possible deuterium substitutions for each of the ^1H hydrogen atoms. Isotopic substitutions encompassed by the compounds herein include but are not limited to: ^2H or ^3H in place of ^1H , ^{13}C or ^{14}C in place of ^{12}C , ^{15}N in place of ^{14}N , ^{17}O or ^{18}O in place of ^{16}O , and ^{33}S , ^{34}S , ^{35}S , or ^{36}S in place of ^{32}S . In certain embodiments, non-radioactive isotopic substitutions may impart new properties on the oligomeric compound that are beneficial for use as a therapeutic or research tool. In certain embodiments, radioactive isotopic substitutions may make the compound suitable for research or diagnostic purposes such as imaging.

EXAMPLES

The following examples illustrate certain embodiments of the present disclosure and are not limiting. Moreover, where specific embodiments are provided, the inventors have contemplated generic application of those specific embodiments. For example, disclosure of an oligonucleotide having a particular motif provides reasonable support for additional oligonucleotides having the same or similar motif. And, for example, where a particular high-affinity modification appears at a particular position, other high-affinity modifications at the same position are considered suitable, unless otherwise indicated.

Example 1: Design and Effect of 3-10-3 cEt gapmers complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 16 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkddddd kkk; wherein "k" represents a cEt sugar moiety, and "d" represents a 2'- β -D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to

SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

- 5 Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (forward sequence ACGAACCTGAAGCCTAAGAAATATCT, designated herein as SEQ ID NO: 10; reverse sequence GAGCACTTGACAGGATGGAACAT, designated herein as SEQ ID NO: 11; probe sequence TGCTCCCAGTTTCTTGAGATCTGCTGACA, designated herein as SEQ ID NO: 12).
- 10 SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 1

15 3-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1482139	26459	26474	28525	28540	GAATCCAGTACATGCT	15	A	13
1482616	20703	20718	22769	22784	TAGTATATGCCACTCG	14	A	14
1482985	87566	87581	89632	89647	GCTCATTTATGCTCAG	22	A	15
1483085	48870	48885	50936	50951	AGGAAGGTAAAGGTTT	11	A	16
1483105	2619	2634	4685	4700	TTTACACCACACTGGA	30	A	17
1483566	22394	22409	24460	24475	GACAATTTCTCTTGA	38	A	18
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	8	A	19
1483873	40141	40156	42207	42222	GTAGAATGCATCTCAA	11	A	20
1484033	2647	2662	4713	4728	ATGAATACATCCATGG	12	A	21
1484219	85814	85829	87880	87895	GCTCATGCATACCCAC	36	A	22
1484486	33023	33038	35089	35104	CATAGAGAATTCTTGC	29	A	23
1484502	25067	25082	27133	27148	ACCATATGATGTATCA	10	A	24
1484517	22966	22981	25032	25047	TATGAAGTGAATTCCA	24	A	25
1484552	37350	37365	39416	39431	ATCAATGCACTCCTTT	41	A	26
1484600	19280	19295	21346	21361	GATAACTCATTTGTCC	18	A	27
1484634	26063	26078	28129	28144	CATACTGCAACAATAG	23	A	28
1484657	71143	71158	73209	73224	AACAAAGATCCTTCAG	37	A	29
1484683	38848	38863	40914	40929	AAGTCTTAAGTTTATG	23	A	30
1484701	102203	102218	104269	104284	GTATTTAATTGCATCC	35	A	31
1484814	49217	49232	51283	51298	CCAAAATATAGCTACA	34	A	32
1484896	46098	46113	48164	48179	GCCTTTATTTTACAC	29	A	33
1484955	27289	27304	29355	29370	GTACTATAACCAGAGA	16	A	34
1484990	27634	27649	29700	29715	AGATTAAGACAACAGC	15	A	35

1485007	39788	39803	41854	41869	GTCTATCAGATCACAC	21	A	36
1485081	46432	46447	48498	48513	GAGTAACACATCCTCT	35	A	37
1485099	21769	21784	23835	23850	GCAAAATTATCATGCC	37	A	38
1485123	28996	29011	31062	31077	GTAACATAATCTGGCTA	29	A	39
1485153	21399	21414	23465	23480	CTCTATATCTAAGCAG	19	A	40
1485164	19608	19623	21674	21689	ATAGTAGCATTACAGA	28	A	41
1485169	21127	21142	23193	23208	CCATATGTTACTCAGT	7	A	42
1485207	93690	93705	95756	95771	TAGAACGTCCACTAGA	45	A	43
1485303	70749	70764	72815	72830	TCCTTAGATCTACATC	44	A	44
1485367	39364	39379	41430	41445	ATGTTATAGTTTCTAC	30	A	45
1485375	23834	23849	25900	25915	GCTATTAAACACAGAC	13	A	46
1485391	43663	43678	45729	45744	GTCAAAATATTCTTAC	20	A	47
1485396	31401	31416	33467	33482	ATCCAAATTTGTCTGG	35	A	48
1485402	36312	36327	38378	38393	TGTGAAATCACCAAGG	23	A	49
1485403	41066	41081	43132	43147	GCAAGGAACTACAGC	21	A	50
1485432	28332	28347	30398	30413	CTAGTTACTATTAAGA	35	A	51
1485469	24380	24395	26446	26461	GTAACATTCCTCTTA	24	A	52
1485471	38240	38255	40306	40321	GGGATAAATAGTCATA	52	A	53
1485502	16106	16121	18172	18187	ACCGTAATCTCACCAG	8	A	54
1485581	20264	20279	22330	22345	AGCCCAACATGACAGC	38	A	55
1485587	33870	33885	35936	35951	GAGTAGAACACTTTTT	10	A	56
1485603	23275	23290	25341	25356	ATATATACTCAATCCA	11	A	57
1485604	44942	44957	47008	47023	GGGAATATACTCAGAC	9	A	58
1485617	17614	17629	19680	19695	AGACACTAGACATGTA	30	A	59
1485634	72189	72204	74255	74270	GTCTAGAATCATTCTG	19	A	60
1485732	47315	47330	49381	49396	GTAATTTTTACCTGGC	21	A	61
1485740	45448	45463	47514	47529	ACATTATTTGCCTAGC	27	A	62
1485829	33472	33487	35538	35553	TACAACCTAACCACGGC	23	A	63
1485897	18630	18645	20696	20711	AACAATTTTCTAGTAG	28	A	64
1485932	86323	86338	88389	88404	AGAACAATTGTACCTA	63	A	65
1485935	57552	57567	59618	59633	TCATTTATAACTGCCA	24	A	66
1485969	32663	32678	34729	34744	ATAACTATTACACAGA	18	A	67
1485987	44543	44558	46609	46624	CCCCTATTATGATGG	69	A	68
1486003	29870	29885	31936	31951	GGAAACAGTCTACATT	23	A	69
1486004	25759	25774	27825	27840	AACCATATTGTTCTGA	9	A	70
1486012	14651	14666	16717	16732	GCACATTTTCTTGACA	47	A	71
1486034	78271	78286	80337	80352	TAGGATTGTACATTGT	17	A	72
1486159	30931	30946	32997	33012	CAGTATAGACTATGGA	4	A	73
1486208	32006	32021	34072	34087	GAGTTAATATCAGCCA	7	A	74
1486250	41565	41580	43631	43646	TGTTAAATGTCACAAG	29	A	75
1486317	37871	37886	39937	39952	TACATAACCAGACTGA	36	A	76
1486319	71789	71804	73855	73870	GTGGAATACAGAACAT	40	A	77
1486327	16701	16716	18767	18782	CCTCATACTGTATTAG	17	A	78
1486364	15583	15598	17649	17664	TATATTTGAACCAGAC	76	A	79
1486366	47984	47999	50050	50065	ACCATTTTATAGCATG	9	A	80

1486367	34754	34769	36820	36835	TGAATATCATGTAGCA	11	A	81
1486442	86878	86893	88944	88959	GAAAGCATTTAACCTA	28	A	82
1486480	30160	30175	32226	32241	AATTTATTTCCACGT	32	A	83
1486527	35340	35355	37406	37421	CCCATATACTCCATTA	43	A	84
1486635	43052	43067	45118	45133	AAGAGAAGCAACCCAC	22	A	85
1486637	44012	44027	46078	46093	GATTCATACTTTGTGT	17	A	86
1486654	48668	48683	50734	50749	GAACCTATTTCCACCA	8	A	87
1486660	40489	40504	42555	42570	GAACATATGCTTCCAT	11	A	88
1486673	18176	18191	20242	20257	TCCATAACTGAATGTA	8	A	89
1486701	36801	36816	38867	38882	TATAATAATCACTGAC	26	A	90
1482285	40154	40169	42220	42235	GCAATAGTTACATGTA	18	B	91
1483061	15585	15600	17651	17666	GTTATATTTGAACCAG	32	B	92
1483214	21128	21143	23194	23209	CCCATATGTTACTCAG	4	B	93
1483225	14771	14786	16837	16852	ACAACCACATGATCTC	168	B	94
1483425	45449	45464	47515	47530	CACATTATTTGCCTAG	29	B	95
1483531	86903	86918	88969	88984	TGTTATATACTTTGGT	8	B	96
1483714	21410	21425	23476	23491	GAAGTATTTGTCTCTA	8	B	97
1483763	48871	48886	50937	50952	GAGGAAGGTAAAGGTT	32	B	98
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	5	B	19
1484099	2648	2663	4714	4729	CATGAATACATCCATG	44	B	99
1484249	20704	20719	22770	22785	ATAGTATATGCCACTC	15	B	100
1484281	40513	40528	42579	42594	ATAATTCTGTACAAGT	18	B	101
1484346	33903	33918	35969	35984	GACTATCAGTATCTGT	12	B	102
1484522	26461	26476	28527	28542	ATGAATCCAGTACATG	14	B	103
1484540	16721	16736	18787	18802	AAACTTCAACGTTGTT	22	B	104
1484545	78407	78422	80473	80488	TCAGTACAATGTCTCA	11	B	105
1484593	43664	43679	45730	45745	GGTCAAAATATTCTTA	10	B	106
1484602	44958	44973	47024	47039	ATTAATTGTTACCTGG	13	B	107
1484648	19281	19296	21347	21362	AGATAACTCATTTGTC	14	B	108
1484682	93856	93871	95922	95937	GAATGATTCATCTTCA	45	B	109
1484714	27290	27305	29356	29371	TGTACTATAACCAGAG	9	B	110
1484737	64423	64438	66489	66504	ACTTAGTCATTCTTCA	37	B	111
1484749	43092	43107	45158	45173	ATCATAACTTTTACTC	18	B	112
1484754	21784	21799	23850	23865	TCATTAATGAAACCAG	8	B	113
1484777	32008	32023	34074	34089	AAGAGTTAATATCAGC	5	B	114
1484850	36368	36383	38434	38449	CAATCTACACAGGCAT	22	B	115
1484876	18177	18192	20243	20258	GTCCATAACTGAATGT	9	B	116
1484884	86324	86339	88390	88405	AAGAACAATTGTACCT	77	B	117
1484889	44017	44032	46083	46098	GTGTAGATTCATACTT	24	B	118
1484891	31412	31427	33478	33493	TTCAAGCTAATATCCA	16	B	119
1484912	39795	39810	41861	41876	TTAAATAGTCTATCAG	34	B	120
1484921	38241	38256	40307	40322	AGGGATAAATAGTCAT	69	B	121
1484975	29873	29888	31939	31954	GAAGGAAACAGTCTAC	28	B	122
1484998	49218	49233	51284	51299	TCCAAAATATAGCTAC	23	B	123
1485093	37354	37369	39420	39435	CTACATCAATGCACCTC	24	B	124

1485122	24383	24398	26449	26464	ATGGTAACTATTCCTC	17	B	125
1485212	19611	19626	21677	21692	CGCATAGTAGCATTAC	13	B	126
1485220	20301	20316	22367	22382	CCATAACACTCAAGTG	11	B	127
1485236	18632	18647	20698	20713	TCAACAATTTTCTAGT	10	B	128
1485276	33024	33039	35090	35105	GCATAGAGAATTCCTG	10	B	129
1485389	35370	35385	37436	37451	GGAATAATTGTACTGA	5	B	130
1485401	47985	48000	50051	50066	CACCATTTTATAGCAT	17	B	131
1485448	48669	48684	50735	50750	AGAACTTATTTCCACC	9	B	132
1485506	25074	25089	27140	27155	CGTTTAGACCATATGA	11	B	133
1485557	22968	22983	25034	25049	CCTATGAACTGAATTC	19	B	134
1485606	23836	23851	25902	25917	AAGCTATTAAACACAG	13	B	135
1485649	22411	22426	24477	24492	ACCAAAAGACCTCTTT	26	B	136
1485753	26065	26080	28131	28146	CACATACTGCAACAAT	29	B	137
1485823	16107	16122	18173	18188	AACCGTAATCTCACCA	11	B	138
1485832	32704	32719	34770	34785	TGAGATTTAATATGGG	13	B	139
1485834	85840	85855	87906	87921	TCCCCAATAAACTTCA	77	B	140
1485857	44568	44583	46634	46649	TGTTATTCTACCACCC	36	B	141
1485885	39381	39396	41447	41462	GATACAACCTTATTCAA	7	B	142
1485940	102506	102521	104572	104587	GATACTCTGATTTCTC	33	B	143
1485989	46141	46156	48207	48222	GTAGATAAAAAGTATC	41	B	144
1486017	30161	30176	32227	32242	TAATTTATTTCCACG	16	B	145
1486035	36899	36914	38965	38980	GTACATATCAAAGTAT	52	B	146
1486039	41635	41650	43701	43716	TATGAATAGCCTTTGT	40	B	147
1486050	72234	72249	74300	74315	GTGAATAGAACTCTGT	30	B	148
1486062	71165	71180	73231	73246	GAACACTTGTATTGGT	14	B	149
1486089	25760	25775	27826	27841	TAACCATATTGTTCTG	9	B	150
1486109	70750	70765	72816	72831	ATCCTTAGATCTACAT	28	B	151
1486143	87577	87592	89643	89658	AAGAGATTCATGCTCA	32	B	152
1486165	71804	71819	73870	73885	TTAAAAGTACTAGCTGG	19	B	153
1486176	47316	47331	49382	49397	AGTAATTTTACCTGG	19	B	154
1486227	23276	23291	25342	25357	AATATATACTCAATCC	18	B	155
1486236	34755	34770	36821	36836	GTGAATATCATGTAGC	6	B	156
1486280	17634	17649	19700	19715	TCATTAGCATCCATTG	23	B	157
1486396	37872	37887	39938	39953	TTACATAACCAGACTG	27	B	158
1486413	30932	30947	32998	33013	TCAGTATAGACTATGG	7	B	159
1486443	27797	27812	29863	29878	GACAAGACACCATCTT	19	B	160
1486459	46433	46448	48499	48514	AGAGTAACACATCCTC	21	B	161
1486570	28998	29013	31064	31079	TTGTAACTAATCTGGC	29	B	162
1486598	28334	28349	30400	30415	TGCTAGTTACTATTAA	27	B	163
1486649	33473	33488	35539	35554	GTACAACCTAACCACGG	13	B	164
1486687	38882	38897	40948	40963	GATACTGAATTTCTG	15	B	165
1486700	41196	41211	43262	43277	GAAGGTACACCTCTTG	27	B	166
1483819	22008	22023	24074	24089	AGATTTTAGGCACTGA	8	AE	167
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	6	AE	168
1534175	5065	5080	7131	7146	GTTAAGTACGCTTCCC	68	AE	169

1534177	39838	39853	41904	41919	GTAGACATAATAATCG	20	AE	170
1534179	22614	22629	24680	24695	TCATATACGAGTTGAC	16	AE	171
1534181	116666	116681	118732	118747	CGAACATTACTGCATC	45	AE	172
1534183	86837	86852	88903	88918	TACAAGTAGGTAGGTC	24	AE	173
1534189	121572	121587	N/A	N/A	TAGGATGCAATTCACC	111	AE	174
1534191	104487	104502	106553	106568	TGTTTTACGAACAGTG	16	AE	175
1534195	73937	73952	76003	76018	TCAAGTAAGGTTGTCC	17	AE	176
1534199	130513	130528	N/A	N/A	AATTCGAGAGGATCTG	78	AE	177
1534203	56339	56354	58405	58420	CTCTATCCCAGAGCGC	9	AE	178
1534207	83550	83565	85616	85631	TCGAATAATAAGATTC	38	AE	179
1534213	94635	94650	96701	96716	CCATATCAGTCTTACG	24	AE	180
1534217	48580	48595	50646	50661	CGTTATGTCATGAAAC	10	AE	181
1534219	67401	67416	69467	69482	TTTATTCACACTCGGA	22	AE	182
1534225	47899	47914	49965	49980	TAACGATTTGTGTGCT	13	AE	183
1534229	33425	33440	35491	35506	GTATACGGAGAAATGG	10	AE	184
1534231	19174	19189	21240	21255	CTCGATTTATTGGTTG	6	AE	185
1534233	23171	23186	25237	25252	GGGCAATTTTCGATT	17	AE	186
1534239	19051	19066	21117	21132	GGTGAAAACCGGTGCC	11	AE	187
1534245	13539	13554	15605	15620	CATGTAGCAATAATCG	49	AE	188
1534247	15671	15686	17737	17752	TTAACGATCAGGAATG	56	AE	189
1534253	63391	63406	65457	65472	ATCGATTAAGTGGAGA	19	AE	190
1534259	41386	41401	43452	43467	TACAATCATATGCACT	21	AE	191
1534263	29173	29188	31239	31254	TAGATAATTGGGAAGT	11	AE	192
1534264	26367	26382	28433	28448	GTTACTTAGTTGCAAA	16	AE	193
1534265	33027	33042	35093	35108	CTCGCATAGAGAATTC	11	AE	194
1534279	55365	55380	57431	57446	GCATTAATCTACAGAC	12	AE	195
1534284	22507	22522	24573	24588	AATACAATTGGCATCT	19	AE	196
1534285	66279	66294	68345	68360	AATATAGTCTCTGGCC	25	AE	197
1534293	37253	37268	39319	39334	TTCCAGATATTGACTA	15	AE	198
1534299	25072	25087	27138	27153	TTTAGACCATATGATG	29	AE	199
1534300	30138	30153	32204	32219	GTACAATAAGTAGTGC	7	AE	200
1534301	24363	24378	26429	26444	ATACAATATTAAGGCC	8	AE	201
1534306	16198	16213	18264	18279	TAAAGGTAGCACTTTT	25	AE	202
1534320	19427	19442	21493	21508	GAAAGGTATGAACTTC	13	AE	203
1534321	19264	19279	21330	21345	TTTAACTAGTCTTATA	53	AE	204
1534324	19555	19570	21621	21636	CTTAGAACAAGCAGAT	23	AE	205
1534329	18578	18593	20644	20659	CTGCGAAAGGTTATCC	8	AE	206
1534332	22621	22636	24687	24702	AATTACTTCATATACG	43	AE	207
1534334	22011	22026	24077	24092	AGTAGATTTTAGGCAC	8	AE	208
1534339	41389	41404	43455	43470	ACTTACAATCATATGC	16	AE	209
1534341	26509	26524	28575	28590	GTTTTAACCAGTGCGG	11	AE	210
1534346	30934	30949	33000	33015	AATCAGTATAGACTAT	29	AE	211
1534348	27933	27948	29999	30014	AGGTAATAAAGTCACG	7	AE	212
1534361	29177	29192	31243	31258	TTATTAGATAATTGGG	9	AE	213
1534362	21481	21496	23547	23562	GTATAGTCATGCATAT	14	AE	214

1534364	34752	34767	36818	36833	AATATCATGTAGCATG	9	AE	215
1534366	32427	32442	34493	34508	GCTCGAATCATTACTG	28	AE	216
1534372	17126	17141	19192	19207	GAATAACACTTTGGCA	13	AE	217
1534380	30889	30904	32955	32970	TTAATCTTGATCAATA	36	AE	218
1534381	55361	55376	57427	57442	TAATCTACAGACACGG	6	AE	219
1534385	85914	85929	87980	87995	TTAACTCAATAGGTAT	23	AE	220
1534386	21133	21148	23199	23214	AGCCACCCATATGTTA	21	AE	221
1534389	24361	24376	26427	26442	ACAATATTAAGGCCTT	15	AE	222
1534391	26514	26529	28580	28595	CATAAGTTTTAACCAG	7	AE	223
1534392	32420	32435	34486	34501	TCATTACTGGTTGCTA	11	AE	224
1534394	30144	30159	32210	32225	ATCCATGTACAATAAG	27	AE	225
1534401	66281	66296	68347	68362	TCAATATAGTCTCTGG	15	AE	226
1534406	18729	18744	20795	20810	TTTTAGCATCCCATAG	34	AE	227
1534409	25055	25070	27121	27136	ATCATATTGTAGATTC	6	AE	228
1534421	41668	41683	43734	43749	GGCAAATATTGTAACC	7	AE	229
1534422	25066	25081	27132	27147	CCATATGATGTATCAT	11	AE	230
1534428	18575	18590	20641	20656	CGAAAGGTTATCCAGT	7	AE	231
1534430	22994	23009	25060	25075	CAATCCATAATGTAAC	44	AE	232
1534432	30929	30944	32995	33010	GTATAGACTATGGATA	18	AE	233
1534434	27491	27506	29557	29572	AGACAATCCATTATTC	21	AE	234
1534440	26506	26521	28572	28587	TTAACCAGTGCGBAAT	23	AE	235
1534444	26371	26386	28437	28452	AATAGTTACTTAGTTG	12	AE	236
1534446	27996	28011	30062	30077	TCGAAATTCATGTGAT	23	AE	237
1534448	42568	42583	44634	44649	TTATAGGCATAATAAG	48	AE	238
1534451	43699	43714	45765	45780	GTATTATTACTAGAAG	20	AE	239
1534461	35369	35384	37435	37450	GAATAATTGTACTGAG	15	AE	240
1534463	44511	44526	46577	46592	TTCTCAAGGATTCACT	35	AE	241
1534474	33873	33888	35939	35954	TTTGAGTAGAACACTT	15	AE	242
1534479	42562	42577	44628	44643	GCATAATAAGTCATAA	16	AE	243
1534480	41665	41680	43731	43746	AAATATTGTAACCCCC	31	AE	244
1482571	22615	22630	24681	24696	TTCATATACGAGTTGA	14	AF	245
1483398	21412	21427	23478	23493	TGGAAGTATTTGTCTC	5	AF	246
1483650	21485	21500	23551	23566	GGATGTATAGTCATGC	5	AF	247
1484024	22010	22025	24076	24091	GTAGATTTTAGGCACT	5	AF	248
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	3	AF	168
1534185	44351	44366	46417	46432	CTCGATACTGGACATC	48	AF	249
1534187	89895	89910	91961	91976	GATAGTAGTAGAGCAT	11	AF	250
1534193	24832	24847	26898	26913	CATAGGGAATTGGCCT	27	AF	251
1534197	22610	22625	24676	24691	ATACGAGTTGACAAAT	18	AF	252
1534201	23628	23643	25694	25709	AGTTAAACCACGAGCC	13	AF	253
1534205	43565	43580	45631	45646	AAAGTAGCCGCTACTG	67	AF	254
1534209	121299	121314	N/A	N/A	GCACTAATGGTTTGCT	65	AF	255
1534211	49066	49081	51132	51147	TCACAATAGCTTGCCA	21	AF	256
1534215	133848	133863	N/A	N/A	GACCCTTATTCATCAG	106	AF	257
1534221	38647	38662	40713	40728	TAAACTACCGCTGCAC	57	AF	258

1534223	13937	13952	16003	16018	ACAATTCAAAGTTCGA	6	AF	259
1534227	28177	28192	30243	30258	AGTAGAAGTAAACGGG	11	AF	260
1534235	103447	103462	105513	105528	GATACACGCTGCTCTT	35	AF	261
1534237	30906	30921	32972	32987	TTACGAAGACAACCCT	33	AF	262
1534241	5067	5082	7133	7148	ATGTAAAGTACGCTTC	65	AF	263
1534243	63390	63405	65456	65471	TCGATTAAGTGGAGAT	26	AF	264
1534249	129782	129797	N/A	N/A	GGTAAGCTAACAGTTA	110	AF	265
1534251	74648	74663	76714	76729	ATGCATCCGAATATCT	40	AF	266
1534255	111133	111148	113199	113214	ACAGTATCTGGATAGC	13	AF	267
1534257	19091	19106	21157	21172	CTAGAGGGTGATGGAC	35	AF	268
1534260	33493	33508	35559	35574	TACAATTTGGCAGGGA	16	AF	269
1534261	18576	18591	20642	20657	GCGAAAGGTTATCCAG	16	AF	270
1534262	29183	29198	31249	31264	AGACAGTTATTAGATA	43	AF	271
1534266	26508	26523	28574	28589	TTTAAACCAGTGCGGA	16	AF	272
1534267	26516	26531	28582	28597	TACATAAGTTTTAACC	22	AF	273
1534268	26513	26528	28579	28594	ATAAGTTTTAACCAGT	13	AF	274
1534280	55367	55382	57433	57448	TAGCATTAAATCTACAG	15	AF	275
1534281	25068	25083	27134	27149	GACCATATGATGTATC	19	AF	276
1534282	33038	33053	35104	35119	ATAGAGATCCTCTCGC	22	AF	277
1534288	22993	23008	25059	25074	AATCCATAATGTAAC	17	AF	278
1534289	26375	26390	28441	28456	CAGTAATAGTTACTTA	39	AF	279
1534291	85912	85927	87978	87993	AACTCAATAGGTATTC	38	AF	280
1534304	66283	66298	68349	68364	TGTCAATATAGTCTCT	23	AF	281
1534308	27995	28010	30061	30076	CGAAATTCATGTGATA	10	AF	282
1534310	20963	20978	23029	23044	TTAAGGGTCATTAGAA	29	AF	283
1534313	45056	45071	47122	47137	TAACTATATCCAGGTG	6	AF	284
1534314	19428	19443	21494	21509	TGAAAGGTATGAACTT	18	AF	285
1534319	27493	27508	29559	29574	CAAGACAATCCATTAT	21	AF	286
1534322	30211	30226	32277	32292	CAAGATTTATCTCATG	8	AF	287
1534326	18738	18753	20804	20819	ATCCAGATTTTTAGC	29	AF	288
1534327	18623	18638	20689	20704	TTCTAGTAGAGCTTCC	15	AF	289
1534340	25709	25724	27775	27790	TATGAAACATCAGCTG	39	AF	290
1534342	30935	30950	33001	33016	AAATCAGTATAGACTA	14	AF	291
1534344	19265	19280	21331	21346	CTTTAACTAGTCTTAT	48	AF	292
1534350	30139	30154	32205	32220	TGTACAATAAGTAGTG	12	AF	293
1534352	41666	41681	43732	43747	CAAATATTGTAACCCC	25	AF	294
1534354	33022	33037	35088	35103	ATAGAGAATTCCTGCT	22	AF	295
1534359	16201	16216	18267	18282	ATATAAAGGTAGCACT	19	AF	296
1534360	39948	39963	42014	42029	GTTAAGCATTGAGATA	12	AF	297
1534368	24362	24377	26428	26443	TACAATATTAAGGCCT	20	AF	298
1534370	22997	23012	25063	25078	TCACAATCCATAATGT	11	AF	299
1534374	85916	85931	87982	87997	CATTAAGTCAATAGGT	26	AF	300
1534379	66280	66295	68346	68361	CAATATAGTCTCTGGC	4	AF	301
1534399	19262	19277	21328	21343	TAAGTCTTATACT	41	AF	302
1534400	35372	35387	37438	37453	GTGGAATAATTGTA	25	AF	303

1534403	22012	22027	24078	24093	AAGTAGATTTTAGGCA	13	AF	304
1534410	66277	66292	68343	68358	TATAGTCTCTGGCCAA	38	AF	305
1534412	41387	41402	43453	43468	TTACAATCATATGCAC	34	AF	306
1534415	72010	72025	74076	74091	AGTTATTGCTATCAAG	7	AF	307
1534419	29176	29191	31242	31257	TATTAGATAATTGGGA	45	AF	308
1534420	34750	34765	36816	36831	TATCATGTAGCATGAT	68	AF	309
1534424	48471	48486	50537	50552	AGTTATTCTCAGCGGT	3	AF	310
1534439	42564	42579	44630	44645	AGGCATAATAAGTCAT	9	AF	311
1534441	41669	41684	43735	43750	AGGCAAATATTGTAAC	22	AF	312
1534442	26368	26383	28434	28449	AGTTACTTAGTTGCAA	4	AF	313
1534454	25057	25072	27123	27138	GTATCATATTGTAGAT	12	AF	314
1534459	30930	30945	32996	33011	AGTATAGACTATGGAT	6	AF	315
1534460	18568	18583	20634	20649	TTATCCAGTCAGGTGG	11	AF	316
1534462	41390	41405	43456	43471	CACTTACAATCATATG	19	AF	317
1534465	55363	55378	57429	57444	ATTAATCTACAGACAC	44	AF	318
1534468	32422	32437	34488	34503	AATCATTACTGGTTGC	18	AF	319
1534470	34753	34768	36819	36834	GAATATCATGTAGCAT	14	AF	320
1534471	16111	16126	18177	18192	AATGAACCGTAATCTC	19	AF	321
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	4	AG	168
1532943	33282	33297	35348	35363	AACGAAGCAAGTTGTC	23	AG	322
1532947	73918	73933	75984	75999	GAAGCCATGTTACCCC	53	AG	323
1532949	30907	30922	32973	32988	GTTACGAAGACAACCC	44	AG	324
1532997	101854	101869	103920	103935	GGCAATATGCAGACGA	10	AG	325
1533017	3337	3352	5403	5418	GAGATTAGTAGCAGCC	50	AG	326
1533033	113581	113596	115647	115662	TATATCCTAACCGCCA	76	AG	327
1533053	127324	127339	N/A	N/A	GTAGAATAACTCTTGG	100	AG	328
1533087	28762	28777	30828	30843	TGAACATACCCTACAC	76	AG	329
1533095	15841	15856	17907	17922	CACTAGCCATCGGCTT	68	AG	330
1533127	30339	30354	32405	32420	GCCTAATAGTGGATGC	31	AG	331
1533153	25162	25177	27228	27243	TGAAATATGGCGGACA	25	AG	332
1533167	36272	36287	38338	38353	TAGCGAAGGACTATAT	23	AG	333
1533217	49191	49206	51257	51272	GGCTTATAACAAGTGT	46	AG	334
1533225	19613	19628	21679	21694	CACGCATAGTAGCATT	8	AG	335
1533243	74706	74721	76772	76787	GCTAATGTATGGAGTA	13	AG	336
1533257	43964	43979	46030	46045	ATTCGCTAGGAGAAAC	24	AG	337
1533265	31665	31680	33731	33746	ACACTAGACGAATGCA	22	AG	338
1533289	7707	7722	9773	9788	GAGTAGCATATGACCC	50	AG	339
1533301	68514	68529	70580	70595	CGTTTAGATATACCTC	41	AG	340
1533309	21519	21534	23585	23600	TATCATCGCAATCAGT	16	AG	341
1533355	109593	109608	111659	111674	ATATCAATTGTCGCAA	68	AG	342
1533371	53505	53520	55571	55586	CTATCAATCGGTACTT	52	AG	343
1533385	17900	17915	19966	19981	CTATTAGCCCGTGAAA	51	AG	344
1533407	55626	55641	57692	57707	AGGAAAGACGGATTGG	15	AG	345
1533411	28004	28019	30070	30085	TAGTATGGTCGAAATT	40	AG	346
1533421	18709	18724	20775	20790	GACCACAATTGCAGAC	11	AG	347

1533433	125293	125308	N/A	N/A	GTCAATTTACTTAGCG	125	AG	348
1533435	5963	5978	8029	8044	AATAGGTGCCAAGTGG	37	AG	349
1533455	106340	106355	108406	108421	TGCTATTAAAGGTTTCG	30	AG	350
1533467	32855	32870	34921	34936	CGACAGATTTAGTGTC	94	AG	351
1533469	31221	31236	33287	33302	GCTCAAACGATTTCAC	31	AG	352
1533475	118610	118625	N/A	N/A	ACGCCTTACACAACAC	78	AG	353
1533491	47900	47915	49966	49981	TTAACGATTTGTGTGC	37	AG	354
1533499	130145	130160	N/A	N/A	TGTACTAGCCTGTGCA	104	AG	355
1533507	126247	126262	N/A	N/A	AAGTTAGTGATGCCAT	100	AG	356
1533513	83460	83475	85526	85541	GCACTATTTGTAGACC	40	AG	357
1533519	52372	52387	54438	54453	CCGACATACATCTCCA	13	AG	358
1533529	115277	115292	117343	117358	CCATTAGTGTGTGGAC	65	AG	359
1533531	107052	107067	109118	109133	ACGGAACCTAAGACTGA	47	AG	360
1533553	120456	120471	N/A	N/A	GGTGAATAGCACTTGT	40	AG	361
1533609	26285	26300	28351	28366	CGTTAAAGAGGTAAGG	35	AG	362
1533619	42626	42641	44692	44707	AATACCTGCCTTCGGA	71	AG	363
1533621	65363	65378	67429	67444	GATCATGCATAGTTCC	23	AG	364
1533623	134664	134679	N/A	N/A	TGTACCTAGACCTCTC	102	AG	365
1533649	40354	40369	42420	42435	CTCCTATGCCGTATTG	35	AG	366
1533673	22612	22627	24678	24693	ATATACGAGTTGACAA	40	AG	367
1533689	39410	39425	41476	41491	AAGAACC GG GTGAATT	30	AG	368
1533691	117942	117957	N/A	N/A	AGTATAGCTAAGTCTA	74	AG	369
1533699	44426	44441	46492	46507	CCCTACAGTAGAAGTG	61	AG	370
1533738	12218	12233	14284	14299	CCATACTAGTTATGAC	57	AG	371
1533757	28113	28128	30179	30194	CGTCAGACAGGTTAAC	25	AG	372
1533769	121991	122006	N/A	N/A	CAAGATTCTACTAGCC	99	AG	373
1533795	86530	86545	88596	88611	AAACATCCGATATTGG	27	AG	374
1533797	93762	93777	95828	95843	ATAATTTGGTGTGCGAG	21	AG	375
1533807	15107	15122	17173	17188	GTACGAATAACAGCAT	58	AG	376
1533811	19049	19064	21115	21130	TGAAAACCGGTGCCAT	37	AG	377
1533881	85433	85448	87499	87514	TATGCTAGATTTGCAC	54	AG	378
1533931	37010	37025	39076	39091	TCCTAACCCGGTCTAA	73	AG	379
1533948	89815	89830	91881	91896	TTAACTACTGAATCGG	14	AG	380
1533950	43566	43581	45632	45647	TAAAGTAGCCGCTACT	77	AG	381
1533967	23627	23642	25693	25708	GTAAACCACGAGCCG	32	AG	382
1533973	132718	132733	N/A	N/A	GACTATGTTAGGACTG	112	AG	383
1533990	14921	14936	16987	17002	TGAGATACGGTCATTC	56	AG	384
1533992	28178	28193	30244	30259	CAGTAGAAGTAAACGG	38	AG	385
1534013	38808	38823	40874	40889	ACATTAGAACGAGGAT	19	AG	386
1534033	24715	24730	26781	26796	CTACTTAGACCTGCC	47	AG	387
1534047	132274	132289	N/A	N/A	GTTCTAATATCAATCC	102	AG	388
1534051	46686	46701	48752	48767	GAACATCACGACATTT	33	AG	389
1534065	26498	26513	28564	28579	TGCGGAATATTGTAAT	22	AG	390
1534076	19869	19884	21935	21950	GGATATGATAACGAAG	10	AG	391
1534085	97877	97892	99943	99958	GATACTAATCCCTCCC	44	AG	392

1534091	34062	34077	36128	36143	CAGGAAAGTTTCACGC	13	AG	393
1534093	71650	71665	73716	73731	TCTAAACGGTGCAGGA	47	AG	394
1534095	25365	25380	27431	27446	GAGCAAGGCCGGCAGT	15	AG	395
1534133	77387	77402	79453	79468	GGTACTAGATCTCTAA	10	AG	396
1534153	111202	111217	113268	113283	CCAGTTGAAAATTTTCG	40	AG	397
1534159	38645	38660	40711	40726	AACTACCGCTGCACAG	41	AG	398
1482502	34331	34346	36397	36412	GTATAGTTTACGTTTCG	12	AH	399
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	18	AH	168
1532955	73936	73951	76002	76017	CAAGTAAGGTTGTCCT	42	AH	400
1532977	8383	8398	10449	10464	CGGTATACTGTGGTAA	30	AH	401
1533005	133002	133017	N/A	N/A	GTACTTAGTGGTGGGA	92	AH	402
1533047	38809	38824	40875	40890	AACATTAGAACGAGGA	24	AH	403
1533055	43567	43582	45633	45648	ATAAAGTAGCCGCTAC	67	AH	404
1533069	30908	30923	32974	32989	AGTTACGAAGACAACC	28	AH	405
1533075	125314	125329	N/A	N/A	TTATCCATTTGGGACC	96	AH	406
1533089	56193	56208	58259	58274	TTCCATTTGAGAACAG	14	AH	407
1533113	19644	19659	21710	21725	GACCAAGTGTTCTAGT	9	AH	408
1533135	26379	26394	28445	28460	GACCCAGTAATAGTTA	36	AH	409
1533175	42627	42642	44693	44708	CAATACCTGCCTTCGG	32	AH	410
1533177	28006	28021	30072	30087	ACTAGTATGGTCGAAA	25	AH	411
1533187	121297	121312	N/A	N/A	ACTAATGGTTTGCTAG	99	AH	412
1533198	31226	31241	33292	33307	ATCTAGCTCAAACGAT	73	AH	413
1533203	22613	22628	24679	24694	CATATACGAGTTGACA	33	AH	414
1533219	106492	106507	108558	108573	TAGTTTAAAGTGGGCTA	62	AH	415
1533237	95339	95354	97405	97420	GTACTACTACTTGTCA	41	AH	416
1533312	19978	19993	22044	22059	ATAACATCGCTGAACC	29	AH	417
1533327	44544	44559	46610	46625	GCCCACTATTATGATG	78	AH	418
1533331	31666	31681	33732	33747	AACACTAGACGAATGC	22	AH	419
1533353	114006	114021	116072	116087	GCCGACCGTGGAGTCA	34	AH	420
1533373	86777	86792	88843	88858	TCCGAAGGACAAAAGC	17	AH	421
1533381	52375	52390	54441	54456	TAGCCGACATACATCT	35	AH	422
1533387	38646	38661	40712	40727	AACTACCGCTGCACA	52	AH	423
1533399	24792	24807	26858	26873	CCTTAATGGACTGTCC	42	AH	424
1533415	116972	116987	N/A	N/A	GCAGATCAACTATACG	47	AH	425
1533419	117943	117958	N/A	N/A	GAGTATAGCTAAGTCT	75	AH	426
1533429	18721	18736	20787	20802	TCCCATAGATGTGACC	8	AH	427
1533463	67251	67266	69317	69332	ACGATATTCTTATATC	44	AH	428
1533487	26507	26522	28573	28588	TTTAACCAGTGCGGAA	40	AH	429
1533489	30400	30415	32466	32481	ATCGGAAGCTCCCTGC	17	AH	430
1533493	25437	25452	27503	27518	ACTCATGAGGCTTGGT	28	AH	431
1533505	111796	111811	113862	113877	AGACTTCGAGATACAC	30	AH	432
1533521	40356	40371	42422	42437	AACTCCTATGCCGTAT	36	AH	433
1533533	121992	122007	N/A	N/A	GCAAGATTCTACTAGC	88	AH	434
1533539	15108	15123	17174	17189	TGTACGAATAACAGCA	39	AH	435
1533589	74762	74777	76828	76843	GGCGATACTAAGCTTA	65	AH	436

1533591	28179	28194	30245	30260	ACAGTAGAAGTAAACG	28	AH	437
1533601	107053	107068	109119	109134	GACGGAACTAAGACTG	31	AH	438
1533611	32865	32880	34931	34946	GATAAATTTGCGACAG	56	AH	439
1533637	89816	89831	91882	91897	CTTAACTACTGAATCG	41	AH	440
1533643	50632	50647	52698	52713	ATGTATGCTACTTCGA	26	AH	441
1533663	3339	3354	5405	5420	GAGAGATTAGTAGCAG	23	AH	442
1533685	23867	23882	25933	25948	ACGCATAATTGAATAC	45	AH	443
1533705	43967	43982	46033	46048	AATATTCGCTAGGAGA	27	AH	444
1533707	37451	37466	39517	39532	ATCATAGTAGCACTCC	7	AH	445
1533713	33424	33439	35490	35505	TATACGGAGAAATGGG	32	AH	446
1533730	36273	36288	38339	38354	CTAGCGAAGGACTATA	40	AH	447
1533745	54244	54259	56310	56325	CCTATCTAGAGGCCAT	39	AH	448
1533763	71651	71666	73717	73732	TTCTAAACGGTGCAGG	17	AH	449
1533773	85464	85479	87530	87545	TAGCTAATCAGGACTC	34	AH	450
1533777	77749	77764	79815	79830	CCAGTATGTTACCCCT	26	AH	451
1533785	134752	134767	N/A	N/A	CAGTACAGTAGGCTTC	103	AH	452
1533833	28160	28175	30226	30241	AGCTAAAGAGTGTATC	43	AH	453
1533841	17902	17917	19968	19983	TTCTATTAGCCCGTGA	24	AH	454
1533847	101855	101870	103921	103936	AGGCAATATGCAGACG	14	AH	455
1533855	25163	25178	27229	27244	GTGAAATATGGCGGAC	25	AH	456
1533885	130146	130161	N/A	N/A	TTGTACTAGCCTGTGC	100	AH	457
1533895	84094	84109	86160	86175	TGAAACATCGCCTCAG	52	AH	458
1533907	21721	21736	23787	23802	CGTTAGCACATGCACA	29	AH	459
1533939	46692	46707	48758	48773	CACTAGGAACATCACG	54	AH	460
1533941	47903	47918	49969	49984	CTATTAACGATTTGTG	8	AH	461
1533944	109594	109609	111660	111675	TATATCAATTGTGCGCA	34	AH	462
1533946	118623	118638	N/A	N/A	AGAGATTTGGATGACG	77	AH	463
1533971	16110	16125	18176	18191	ATGAACCGTAATCTCA	21	AH	464
1533979	12219	12234	14285	14300	GCCATACTAGTTATGA	63	AH	465
1533983	99952	99967	102018	102033	GACATTAACGATGTGA	21	AH	466
1533998	39824	39839	41890	41905	CGACTTGAATAATGTA	9	AH	467
1534017	29191	29206	31257	31272	TAGTGGTAAGACAGTT	35	AH	468
1534019	19050	19065	21116	21131	GTGAAAACCGGTGCCA	15	AH	469
1534027	127426	127441	N/A	N/A	GACTCATAATGGATAC	105	AH	470
1534035	6023	6038	8089	8104	GTAATTGATGGTTAGC	31	AH	471
1534061	126248	126263	N/A	N/A	CAAGTTAGTGATGCCA	101	AH	472
1534117	69977	69992	72043	72058	CGTACTATTGTCCATA	18	AH	473
1534143	15088	15103	17154	17169	AAACGGTTGTGAAGGA	26	AH	474
1534151	132464	132479	N/A	N/A	GACCATCGCCTTTGTA	65	AH	475
1482506	18242	18257	20308	20323	GACGGTACATGTTTCC	8	AI	476
1483282	47904	47919	49970	49985	GCTATTAACGATTTGT	7	AI	477
1483576	40532	40547	42598	42613	AAGAGTAATGCTATCG	8	AI	478
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	30	AI	168
1532963	46300	46315	48366	48381	AGCGATGGAGTACCTA	11	AI	479
1532967	25549	25564	27615	27630	CATTAGCGAAGTATAA	50	AI	480

1533057	86020	86035	88086	88101	GATTAGCAGATTCCAC	37	AI	481
1533059	125424	125439	N/A	N/A	TAGATAACTAGCTAGG	89	AI	482
1533063	19861	19876	21927	21942	TAACGAAGCTGACTGC	29	AI	483
1533081	50956	50971	53022	53037	TGATTACATTCCGCAT	25	AI	484
1533109	42658	42673	44724	44739	GGCGAGAATTTGCTTT	39	AI	485
1533133	96070	96085	98136	98151	CTCAAGCCGCAATTCC	65	AI	486
1533145	126384	126399	N/A	N/A	ACAATATAGGTTCCCC	87	AI	487
1533173	101409	101424	103475	103490	CGAAGTACAGTAGACC	29	AI	488
1533179	22616	22631	24682	24697	CTTCATATACGAGTTG	7	AI	489
1533191	73938	73953	76004	76019	GTCAAGTAAGGTTGTC	18	AI	490
1533197	121477	121492	N/A	N/A	AATCTTGCGTTCGCG	112	AI	491
1533209	43569	43584	45635	45650	ACATAAAGTAGCCGCT	35	AI	492
1533211	84323	84338	86389	86404	ATCATATGATGCTGTC	29	AI	493
1533231	8389	8404	10455	10470	GACTTTCGGTATACTG	29	AI	494
1533285	25164	25179	27230	27245	GGTGAAATATGGCGGA	16	AI	495
1533295	134910	134925	N/A	N/A	CACATTTAAGCCCTCG	69	AI	496
1533305	4868	4883	6934	6949	GACTACCTTCACACTT	59	AI	497
1533306	26390	26405	28456	28471	CTGTAATCTAGGACCC	8	AI	498
1533319	30404	30419	32470	32485	AGCGATCGGAAGCTCC	25	AI	499
1533329	31671	31686	33737	33752	TAACAAACACTAGACG	44	AI	500
1533337	102097	102112	104163	104178	TACACTTAACGAACCC	25	AI	501
1533339	28181	28196	30247	30262	CGACAGTAGAAGTAAA	35	AI	502
1533341	35174	35189	37240	37255	GGTATAAGGTCATGTA	13	AI	503
1533343	122561	122576	N/A	N/A	GACCGTAAGTTGCTGG	86	AI	504
1533345	111846	111861	113912	113927	CGAAATGCTGAGTGGG	24	AI	505
1533369	87151	87166	89217	89232	GTTAAGTGAAGTAGGT	15	AI	506
1533391	57002	57017	59068	59083	TCGATTAATCAACTGG	6	AI	507
1533431	19979	19994	22045	22060	AATAACATCGCTGAAC	58	AI	508
1533459	36275	36290	38341	38356	TGCTAGCGAAGGACTA	31	AI	509
1533483	117960	117975	N/A	N/A	AAGATATGTGAGTCGA	64	AI	510
1533503	39832	39847	41898	41913	ATAATAATCGACTTGA	37	AI	511
1533525	28168	28183	30234	30249	AAACGGGCAGCTAAAG	55	AI	512
1533541	116986	117001	N/A	N/A	GTTAACCTATAGTTGC	66	AI	513
1533543	29479	29494	31545	31560	AGCCTAGGGTGGTAAC	51	AI	514
1533563	28007	28022	30073	30088	AACTAGTATGGTCGAA	18	AI	515
1533565	38648	38663	40714	40729	CTAAACTACCGCTGCA	58	AI	516
1533567	12222	12237	14288	14303	ATAGCCATACTAGTTA	41	AI	517
1533575	133474	133489	N/A	N/A	GATATCACCTGCGCAT	171	AI	518
1533587	77750	77765	79816	79831	ACCAGTATGTTACCCC	11	AI	519
1533617	15089	15104	17155	17170	GAAACGGTTGTGAAGG	23	AI	520
1533629	46737	46752	48803	48818	TGAGAAGGGCTTTCCG	51	AI	521
1533639	21735	21750	23801	23816	ATACTAACAATAGACG	18	AI	522
1533659	67257	67272	69323	69338	ACATTGACGATATTCT	9	AI	523
1533671	119006	119021	N/A	N/A	GCACCAAGTAACCACC	104	AI	524
1533677	89897	89912	91963	91978	TAGATAGTAGTAGAGC	17	AI	525

1533681	15112	15127	17178	17193	CATATGTACGAATAAC	73	AI	526
1533709	43968	43983	46034	46049	TAATATTCGCTAGGAG	15	AI	527
1533719	19054	19069	21120	21135	AAAGGTGAAAACCGGT	26	AI	528
1533729	33426	33441	35492	35507	AGTATACGGAGAAATG	25	AI	529
1533765	33124	33139	35190	35205	ACCCCATAGCTTATTG	53	AI	530
1533779	30909	30924	32975	32990	AAGTTACGAAGACAAC	19	AI	531
1533799	69980	69995	72046	72061	CTCCGTACTATTGTCC	21	AI	532
1533879	17808	17823	19874	19889	ACGAAGCTATAAATAG	21	AI	533
1533893	23870	23885	25936	25951	GCAACGCATAATTGAA	71	AI	534
1533897	130478	130493	N/A	N/A	CCACATGGCACCCTCG	112	AI	535
1533915	71652	71667	73718	73733	TTTCTAAACGGTGCAG	29	AI	536
1533921	26603	26618	28669	28684	GTCTGAATGAATGTACG	15	AI	537
1533923	38810	38825	40876	40891	CAACATTAGAACGAGG	23	AI	538
1533927	107058	107073	109124	109139	GTTATGACGGAACTAA	45	AI	539
1533929	37559	37574	39625	39640	CTACACCACGGTTTTT	50	AI	540
1533961	127664	127679	N/A	N/A	CTAATCTAGATGGCTC	112	AI	541
	129709	129724						
1533963	114927	114942	116993	117008	AGTTAGCATTGACCCA	43	AI	542
1533994	132472	132487	N/A	N/A	ATAATGCAGACCATCG	119	AI	543
1534029	55362	55377	57428	57443	TTAATCTACAGACACG	86	AI	544
1534037	18722	18737	20788	20803	ATCCCATAGATGTGAC	9	AI	545
1534043	31454	31469	33520	33535	TCGCATATAACCAAAT	13	AI	546
1534053	24833	24848	26899	26914	GCATAGGGAATTGGCC	37	AI	547
1534081	109595	109610	111661	111676	ATATATCAATTGTTCGC	17	AI	548
1534106	52383	52398	54449	54464	ATTTTTTAATAGCCGAC	15	AI	549
1534129	74774	74789	76840	76855	TAGTATCACATTGGCG	60	AI	550
1534131	106493	106508	108559	108574	CTAGTTTAAAGTGGGCT	69	AI	551
1534149	6075	6090	8141	8156	GTATCAAACCAATCAG	29	AI	552
1483739	29585	29600	31651	31666	ATTATTCCGACTGCTC	43	AJ	553
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	8	AJ	168
1532965	18245	18260	20311	20326	AAAGACGGTACATGTT	27	AJ	554
1532971	117079	117094	N/A	N/A	GCCATAGAAACAACGA	81	AJ	555
1532981	38219	38234	40285	40300	ATAAGGCATTGCGGAG	60	AJ	556
1532993	74783	74798	76849	76864	GTGGATACTTAGTATC	42	AJ	557
1533007	30408	30423	32474	32489	CAAGAGCGATCGGAAG	27	AJ	558
1533023	79158	79173	81224	81239	GTAGACTAGATGTGTG	22	AJ	559
1533041	132681	132696	N/A	N/A	GCTTATGGGAAGACCA	66	AJ	560
1533045	47905	47920	49971	49986	TGCTATTAACGATTTG	12	AJ	561
1533079	15670	15685	17736	17751	TAACGATCAGGAATGT	43	AJ	562
1533091	52482	52497	54548	54563	GGTGAATAAACTTCGA	15	AJ	563
1533101	119182	119197	N/A	N/A	CCTATACCTAACAGCC	102	AJ	564
1533107	101410	101425	103476	103491	ACGAAGTACAGTAGAC	62	AJ	565
1533111	102425	102440	104491	104506	ACGAATTATTGAGGTC	26	AJ	566
1533115	38761	38776	40827	40842	GTCAAACGACAAATTC	29	AJ	567
1533125	70146	70161	72212	72227	CAACACATACCTAGGT	61	AJ	568

1533143	123275	123290	N/A	N/A	ATTCCTAGGGTCACG	83	AJ	569
1533155	96346	96361	98412	98427	ATAGATGGGTCTGTCA	37	AJ	570
1533207	22210	22225	24276	24291	ATTTATGCCCCGCACC	47	AJ	571
1533213	133477	133492	N/A	N/A	CCAGATATCACCTGCG	81	AJ	572
1533223	126496	126511	N/A	N/A	ATAATTCCGGTGCTCTA	118	AJ	573
1533267	57214	57229	59280	59295	ACTATTAAGCGATCTG	10	AJ	574
1533269	6770	6785	8836	8851	TCTAATGTATGAGGAC	56	AJ	575
1533273	15090	15105	17156	17171	AGAAACGGTTGTGAAG	67	AJ	576
1533275	33467	33482	35533	35548	CTAACCACGGCACAAT	46	AJ	577
1533297	8815	8830	10881	10896	TATACGATACCTTCA	49	AJ	578
1533315	86021	86036	88087	88102	CGATTAGCAGATTCCA	17	AJ	579
1533317	106494	106509	108560	108575	ACTAGTTTAAAGTGGGC	47	AJ	580
1533335	19094	19109	21160	21175	CAACTAGAGGGTGATG	46	AJ	581
1533367	17814	17829	19880	19895	AATCTTACGAAGCTAT	16	AJ	582
1533375	26391	26406	28457	28472	ACTGTAATCTAGGACC	8	AJ	583
1533377	40578	40593	42644	42659	GCACAATTGTTGATTG	39	AJ	584
1533395	115055	115070	117121	117136	AATATTTCCGGTTCAT	101	AJ	585
1533423	107311	107326	109377	109392	AGTGATCAAACGGGAC	15	AJ	586
1533427	111850	111865	113916	113931	GCACCGAAATGCTGAG	31	AJ	587
1533447	136583	136598	N/A	N/A	CTGATTAGACAGTCTT	90	AJ	588
1533473	73966	73981	76032	76047	AATACCCCTAGTGTC	24	AJ	589
1533501	25550	25565	27616	27631	TCATTAGCGAAGTATA	27	AJ	590
1533511	28169	28184	30235	30250	TAAACGGGCAGCTAAA	63	AJ	591
1533527	72110	72125	74176	74191	CTCGAGATTAGTTCTT	17	AJ	592
1533549	19862	19877	21928	21943	ATAACGAAGCTGACTG	45	AJ	593
1533551	90284	90299	92350	92365	AGCGAATGTCTCTCC	54	AJ	594
1533561	121478	121493	N/A	N/A	TAATCTTGGGTGTTTCG	80	AJ	595
1533571	36844	36859	38910	38925	CTGTATTGGCCCAAT	22	AJ	596
1533579	39836	39851	41902	41917	AGACATAATAATCGAC	17	AJ	597
1533605	44193	44208	46259	46274	TAACACGACACAGTTT	71	AJ	598
1533613	26604	26619	28670	28685	AGTCGAATGAATGTAC	19	AJ	599
1533615	109596	109611	111662	111677	AATATATCAATTGTCTG	37	AJ	600
1533635	38811	38826	40877	40892	ACAACATTAGAACGAG	21	AJ	601
1533679	130492	130507	N/A	N/A	TCAATATTGTCTACCC	108	AJ	602
1533711	28008	28023	30074	30089	CAACTAGTATGGTCGA	8	AJ	603
1533715	30912	30927	32978	32993	AAGAAGTTACGAAGAC	16	AJ	604
1533723	127666	127681	N/A	N/A	GTCTAATCTAGATGGC	68	AJ	605
	129711	129726						
1533727	13538	13553	15604	15619	ATGTAGCAATAATCGA	42	AJ	606
1533734	84421	84436	86487	86502	AACTCCGATGACTCAT	37	AJ	607
1533747	35927	35942	37993	38008	CCTACTATTCTGGTAC	25	AJ	608
1533761	43570	43585	45636	45651	CACATAAAGTAGCCGC	20	AJ	609
1533803	55384	55399	57450	57465	GCTTTTACACCCGATT	12	AJ	610
1533813	67403	67418	69469	69484	AGTTTATTACACTCG	20	AJ	611
1533815	32407	32422	34473	34488	CTATCTAGGGATCACC	41	AJ	612

1533823	43126	43141	45192	45207	CAAACCCGGCATTATT	56	AJ	613
1533825	25195	25210	27261	27276	CTCGGACGGAAGTGAA	48	AJ	614
1533829	46301	46316	48367	48382	TAGCGATGGAGTACCT	41	AJ	615
1533839	18967	18982	21033	21048	CAGTACCCCTACTTGT	26	AJ	616
1533843	31459	31474	33525	33540	AAATTTTCGCATATAAC	45	AJ	617
1533853	87168	87183	89234	89249	CCCAAGTAGTACAATC	26	AJ	618
1533867	125428	125443	N/A	N/A	GTACTAGATAACTAGC	97	AJ	619
1533869	24834	24849	26900	26915	GGCATAGGGAATTGGC	9	AJ	620
1533937	23872	23887	25938	25953	TGGCAACGCATAATTG	67	AJ	621
1533945	5062	5077	7128	7143	AAGTACGCTTCCCCAA	82	AJ	622
1533947	50958	50973	53024	53039	TATGATTACATTCCGC	13	AJ	623
1533949	28183	28198	30249	30264	AACGACAGTAGAAGTA	73	AJ	624
1533989	20720	20735	22786	22801	GATTATAGTGCCAGTA	14	AJ	625
1534049	46959	46974	49025	49040	TAGTATCAGGGTGCAC	37	AJ	626
1534059	33192	33207	35258	35273	CTTAACTACAGGGACC	39	AJ	627
1534089	23091	23106	25157	25172	GATATTAAGGATTGTC	53	AJ	628
1534173	117961	117976	N/A	N/A	GAAGATATGTGAGTCG	32	AJ	629
1483488	28010	28025	30076	30091	GGCAACTAGTATGGTC	5	AK	630
1483906	46302	46317	48368	48383	CTAGCGATGGAGTACC	65	AK	631
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	12	AK	168
1532945	36989	37004	39055	39070	CGTAATTAGTCCCCTT	30	AK	632
1532953	26609	26624	28675	28690	GAATCAGTCGAATGAA	14	AK	633
1532979	134247	134262	N/A	N/A	GACTATCTTGCGCTTC	102	AK	634
1532995	28184	28199	30250	30265	TAACGACAGTAGAAGT	61	AK	635
1533001	127787	127802	N/A	N/A	GAGGATAACCGGCTTG	99	AK	636
1533011	38856	38871	40922	40937	GGTTAGCTAAGTCTTA	20	AK	637
1533031	5064	5079	7130	7145	TTAAGTACGCTTCCCC	90	AK	638
1533037	136794	136809	N/A	N/A	TTTACACGATAGCCTC	107	AK	639
1533073	18247	18262	20313	20328	TAAAAGACGGTACATG	29	AK	640
1533085	118340	118355	N/A	N/A	CCTAATTCCGAGAGAC	64	AK	641
1533105	109771	109786	111837	111852	ATCTATTCGCTGTGTT	45	AK	642
1533117	38766	38781	40832	40847	TATCAGTCAAACGACA	38	AK	643
1533121	117409	117424	N/A	N/A	GAAGTTCCATAGTCTA	72	AK	644
1533131	39853	39868	41919	41934	CGTTAAACTGCATAGG	15	AK	645
1533139	101415	101430	103481	103496	TACACACGAAGTACAG	75	AK	646
1533169	31462	31477	33528	33543	GCAAAATTTTCGCATAT	18	AK	647
1533171	48145	48160	50211	50226	GCCTATCCGAATAACA	57	AK	648
1533185	107324	107339	109390	109405	GTCAATTAGTCTTAGT	33	AK	649
1533195	55500	55515	57566	57581	GACGGATCAGACACTC	17	AK	650
1533201	32409	32424	34475	34490	TGCTATCTAGGGATCA	29	AK	651
1533227	44194	44209	46260	46275	CTAACACGACACAGTT	69	AK	652
1533249	7402	7417	9468	9483	ACGGAGTGGACATGTT	50	AK	653
1533251	25552	25567	27618	27633	TTTCATTAGCGAAGTA	27	AK	654
1533283	51772	51787	53838	53853	TATGACAACAGAACGA	33	AK	655
1533291	43127	43142	45193	45208	TCAAACCCGGCATTAT	45	AK	656

1533299	74888	74903	76954	76969	ATATCTGTAACCACGC	14	AK	657
1533357	125429	125444	N/A	N/A	TGTACTAGATAACTAG	94	AK	658
1533379	87406	87421	89472	89487	GCTTATTGGCTCCACT	27	AK	659
1533393	25203	25218	27269	27284	GATTAGGCCTCGGACG	22	AK	660
1533401	74631	74646	76697	76712	ATTATTGGATATTCGA	39	AK	661
1533405	28170	28185	30236	30251	GTAAACGGGCAGCTAA	33	AK	662
1533409	130908	130923	N/A	N/A	GTAATTAGACCTGGTA	89	AK	663
1533413	111851	111866	113917	113932	AGCACCGAAATGCTGA	68	AK	664
1533437	17818	17833	19884	19899	GTGAAATCTTACGAAG	6	AK	665
1533449	119878	119893	N/A	N/A	GGTAATAAGCTGCTAT	57	AK	666
1533453	121492	121507	N/A	N/A	GACAAGGCACTATGTA	88	AK	667
1533457	35976	35991	38042	38057	TACCCAAGTGGCACAC	8	AK	668
1533465	22211	22226	24277	24292	TATTTATGCCCGTCAC	25	AK	669
1533471	84423	84438	86489	86504	TTAACTCCGATGACTC	43	AK	670
1533477	13913	13928	15979	15994	CCAGCGAAAAGCTGTA	92	AK	671
1533569	23175	23190	25241	25256	GAAAGGGCAATTTTCG	61	AK	672
1533577	70701	70716	72767	72782	TAACCAGTGTGTGGAC	38	AK	673
1533595	43571	43586	45637	45652	TCACATAAAGTAGCCG	10	AK	674
1533607	15672	15687	17738	17753	TTTAACGATCAGGAAT	64	AK	675
1533651	33468	33483	35534	35549	ACTAACCACGGCACAA	56	AK	676
1533653	103129	103144	105195	105210	GCAGAAGCGCACTTTC	52	AK	677
1533669	19863	19878	21929	21944	GATAACGAAGCTGACT	31	AK	678
1533733	115057	115072	117123	117138	ACAATATTTCCGGTTC	83	AK	679
1533781	132703	132718	N/A	N/A	GACGACAGAAGAGTTC	109	AK	680
1533791	25108	25123	27174	27189	GACCCCTGAAGTATTA	54	AK	681
1533809	58785	58800	60851	60866	GCACTAGATTACCCAA	34	AK	682
1533819	126497	126512	N/A	N/A	GATAATTCGGTGCTCT	104	AK	683
1533851	90285	90300	92351	92366	AAGCGAATGTCCTCTC	30	AK	684
1533861	23918	23933	25984	25999	GATGAGTAGCTATGGT	7	AK	685
1533863	26409	26424	28475	28490	AGGAACGCAATAATCC	39	AK	686
1533871	29586	29601	31652	31667	AATTATTCGACTGCT	48	AK	687
1533875	46972	46987	49038	49053	TCACTATGGATGGTAG	13	AK	688
1533877	52600	52615	54666	54681	TATAGGATCAGCTGGC	22	AK	689
1533903	30410	30425	32476	32491	TTCAAGAGCGATCGGA	20	AK	690
1533925	106496	106511	108562	108577	GTACTAGTTTAAGTGG	37	AK	691
1533935	20853	20868	22919	22934	CATTAGTGGGCTCTCA	29	AK	692
1533969	18976	18991	21042	21057	CTAGACATCCAGTACC	34	AK	693
1534023	38220	38235	40286	40301	TATAAGGCATTGCGGA	53	AK	694
1534031	8817	8832	10883	10898	ATTATACGGATACCTT	75	AK	695
1534045	15093	15108	17159	17174	ATAAGAAACGGTTGTG	63	AK	696
1534097	19095	19110	21161	21176	TCAACTAGAGGGTGAT	55	AK	697
1534105	79275	79290	81341	81356	CTAGATATGCACCCCC	42	AK	698
1534108	86023	86038	88089	88104	TCCGATTAGCAGATTC	26	AK	699
1534125	67501	67516	69567	69582	TAAATTGATTACACG	22	AK	700
1534127	124618	124633	N/A	N/A	CGCTTACAAATTTAGC	92	AK	701

1534139	41330	41345	43396	43411	AACCCATGTAACGACC	25	AK	702
1534141	72112	72127	74178	74193	TGCTCGAGATTAGTTC	16	AK	703
1534157	96347	96362	98413	98428	GATAGATGGGTCTGTC	44	AK	704
1534163	33193	33208	35259	35274	CCTTAACTACAGGGAC	48	AK	705
1534165	30917	30932	32983	32998	GATAAAAGAAGTTACG	41	AK	706
1482199	29588	29603	31654	31669	AGAATTATTCCGACTG	19	AL	707
1482343	22212	22227	24278	24293	CTATTTATGCCCCGTC	4	AL	708
1483521	41598	41613	43664	43679	GTAACCTTAGGACAAGG	25	AL	709
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	6	AL	168
1532969	20856	20871	22922	22937	TACCATTAGTGGGCTC	19	AL	710
1532985	106554	106569	108620	108635	ACTGTATTATGTGCC	43	AL	711
1532987	17888	17903	19954	19969	GAAAAGGGTCGGAGAC	17	AL	712
1533009	25205	25220	27271	27286	CAGATTAGGCCTCGGA	14	AL	713
1533021	18252	18267	20318	20333	GTGAATAAAAGACGGT	14	AL	714
1533025	131252	131267	N/A	N/A	TGTAACAGTTGAGTCC	120	AL	715
	131273	131288						
1533043	46977	46992	49043	49058	CCGTATCACTATGGAT	38	AL	716
1533065	30411	30426	32477	32492	TTTCAAGAGCGATCGG	23	AL	717
1533067	117411	117426	N/A	N/A	TCGAAGTTCCATAGTC	87	AL	718
1533071	111922	111937	113988	114003	CGTAGATTGAAGCCAC	29	AL	719
1533083	38767	38782	40833	40848	ATATCAGTCAAACGAC	31	AL	720
1533103	37006	37021	39072	39087	AACCCGGTCTAAACCT	54	AL	721
1533141	46305	46320	48371	48386	ATCCTAGCGATGGAGT	72	AL	722
1533151	132713	132728	N/A	N/A	TGTTAGGACTGACGAC	112	AL	723
1533159	125613	125628	N/A	N/A	CATAGGTTAACAGTGG	99	AL	724
1533205	127919	127934	N/A	N/A	CCAATTGAGTTGAGAT	95	AL	725
1533221	74681	74696	76747	76762	CGAAAAGCATGGGCTT	35	AL	726
1533253	36269	36284	38335	38350	CGAAGGACTATATAAT	30	AL	727
1533255	86523	86538	88589	88604	CGATATTGGAATATTC	22	AL	728
1533259	125046	125061	N/A	N/A	GCGAATTTGTGAACT	101	AL	729
1533261	43167	43182	45233	45248	TTTTTAGGAAGTAGCG	10	AL	730
1533277	15673	15688	17739	17754	GTTTAAACGATCAGGAA	51	AL	731
1533279	19864	19879	21930	21945	TGATAACGAAGCTGAC	42	AL	732
1533321	67784	67799	69850	69865	GCTACGACACAGTAGC	120	AL	733
1533333	96350	96365	98416	98431	GATGATAGATGGGTCT	33	AL	734
1533351	80788	80803	82854	82869	AATCTTCAGGGACTCG	26	AL	735
1533359	32418	32433	34484	34499	ATTACTGGTTGCTATC	20	AL	736
1533363	27099	27114	29165	29180	GCACAACAAATAGGTC	11	AL	737
1533365	84544	84559	86610	86625	GATAAATGTTGCTCCG	27	AL	738
1533383	134416	134431	N/A	N/A	TATACAGCTGGGTTCC	104	AL	739
1533417	63393	63408	65459	65474	AGATCGATTAAAGTGGA	20	AL	740
1533439	30967	30982	33033	33048	CCGAAATACCACCTGA	21	AL	741
1533441	118446	118461	N/A	N/A	GACAAGTATGCACTGC	90	AL	742
1533443	107457	107472	109523	109538	TGGTAGATACGCCTCT	41	AL	743
1533479	13924	13939	15990	16005	CGATTTAAATGCCAGC	18	AL	744

1533485	38913	38928	40979	40994	GATCAACCAGTATTAG	40	AL	745
1533559	24068	24083	26134	26149	GATCATGTATCGACAC	4	AL	746
1533581	90451	90466	92517	92532	CCTAGTAAGTGCCGAG	32	AL	747
1533583	38221	38236	40287	40302	CTATAAGGCATTGCGG	24	AL	748
1533599	44306	44321	46372	46387	TATCCAAGGGCCCACT	60	AL	749
1533627	23495	23510	25561	25576	TTGTAGGAGGACTACC	19	AL	750
1533633	33469	33484	35535	35550	AACTAACCACGGCACA	47	AL	751
1533655	15094	15109	17160	17175	CATAAGAAACGGTTGT	64	AL	752
1533665	33196	33211	35262	35277	TATCCTTAACTACAGG	27	AL	753
1533667	31464	31479	33530	33545	GAGCAAAATTTTCGCAT	11	AL	754
1533683	126500	126515	N/A	N/A	TTTGATAATTCGGTGC	115	AL	755
1533697	48295	48310	50361	50376	GCCTAAGTCTTGGTGC	52	AL	756
1533749	75481	75496	77547	77562	AATACTCATAGTGGGC	14	AL	757
1533753	25635	25650	27701	27716	TGCAAGGGTTATTGTG	39	AL	758
1533771	43961	43976	46027	46042	CGCTAGGAGAAACACT	16	AL	759
1533817	109774	109789	111840	111855	TTAATCTATTCGCTGT	61	AL	760
1533831	52977	52992	55043	55058	CTAATATGTTTGATCG	11	AL	761
1533837	120027	120042	N/A	N/A	GCTTATTCAGTACTCC	90	AL	762
1533865	52014	52029	54080	54095	GGTTTATGTATAATCG	9	AL	763
1533889	87407	87422	89473	89488	AGCTTATTGGCTCCAC	28	AL	764
1533911	72116	72131	74182	74197	AATATGCTCGAGATTA	67	AL	765
1533942	25159	25174	27225	27240	AATATGGCGGACAGAG	40	AL	766
1533943	26410	26425	28476	28491	AAGGAACGCAATAATC	47	AL	767
1533981	28185	28200	30251	30266	CTAACGACAGTAGAAG	72	AL	768
1534009	39912	39927	41978	41993	GCCTAGCAAGTTAGTC	17	AL	769
1534015	71587	71602	73653	73668	ACGCAATCTCTTTAAC	31	AL	770
1534041	28089	28104	30155	30170	CGAAAAGTTGGCATAAC	16	AL	771
1534055	121742	121757	N/A	N/A	GGTAATACAGTGGCTC	93	AL	772
1534057	7409	7424	9475	9490	TTCCTATACGGAGTGG	58	AL	773
1534066	19172	19187	21238	21253	CGATTTATTGGTTGTT	9	AL	774
1534075	137194	137209	N/A	N/A	TACTGTATGGAGTGTT	105	AL	775
1534087	101545	101560	103611	103626	ACAATGTAGTGACCTA	29	AL	776
1534099	28171	28186	30237	30252	AGTAAACGGGCAGCTA	18	AL	777
1534110	19046	19061	21112	21127	AAACCGGTGCCATTAC	39	AL	778
1534121	55506	55521	57572	57587	ATTTTTGACGGATCAG	10	AL	779
1534147	115060	115075	117126	117141	AACACAATATTTCCGG	79	AL	780
1534155	9008	9023	11074	11089	TTTATGGAATCGGCAT	42	AL	781
1534169	103397	103412	105463	105478	GAGCTAGTAAGCTTCA	90	AL	782
1534171	5068	5083	7134	7149	GATGTTAAGTACGCTT	66	AL	783
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	14	AM	168
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	13	AN	168
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	5	AO	168
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	9	AP	168
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	7	AQ	168
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	12	AR	168

1483474	32828	32843	34894	34909	ATTATCATGGTTGCCC	12	AS	784
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	4	AS	168
1532941	117612	117627	N/A	N/A	CTGTACTAGTACTACT	62	AS	785
1532942	44307	44322	46373	46388	ATATCCAAGGGCCAC	23	AS	786
1532951	15674	15689	17740	17755	AGTTTAAACGATCAGGA	15	AS	787
1532961	28187	28202	30253	30268	CTCTAACGACAGTAGA	49	AS	788
1532989	127309	127324	N/A	N/A	GATTAGTGTCTAGTTG	96	AS	789
1532991	39408	39423	41474	41489	GAACCGGGTGAATTTT	16	AS	790
1533003	118484	118499	N/A	N/A	AATTCCTAGGTAGTCG	78	AS	791
1533013	33793	33808	35859	35874	TATGATGCAGTAAGGC	7	AS	792
1533015	115065	115080	117131	117146	TCCGGAACACAATATT	97	AS	793
1533027	23624	23639	25690	25705	AAACCACGAGCCGTC	17	AS	794
1533029	53233	53248	55299	55314	GATACTTTCGGCAGAA	14	AS	795
1533035	132714	132729	N/A	N/A	ATGTTAGGACTGACGA	102	AS	796
1533039	76342	76357	78408	78423	GATAATGTTGGCAAGC	21	AS	797
1533097	43962	43977	46028	46043	TCGCTAGGAGAAACAC	11	AS	798
1533119	24405	24420	26471	26486	CGTCAAAGAGGCATTA	40	AS	799
1533123	19867	19882	21933	21948	ATATGATAACGAAGCT	35	AS	800
1533147	46311	46326	48377	48392	GATATGATCCTAGCGA	11	AS	801
1533157	125680	125695	N/A	N/A	TTAACTAACAGCAGCG	86	AS	802
1533161	48460	48475	50526	50541	GCGGTAAGTTTTCTTA	7	AS	803
1533163	30969	30984	33035	33050	ACCCGAAATACCACCT	25	AS	804
1533181	55507	55522	57573	57588	TATTTTGTACGGATCA	12	AS	805
1533183	106973	106988	109039	109054	TAGGTTAGGTGAGTGT	36	AS	806
1533215	19602	19617	21668	21683	GCATTACAGAATAACG	5	AS	807
1533241	18432	18447	20498	20513	ATACTACCTATAAGGG	33	AS	808
1533245	31662	31677	33728	33743	CTAGACGAATGCAAAT	39	AS	809
1533271	72120	72135	74186	74201	CAAAAATATGCTCGAG	11	AS	810
1533311	90609	90624	92675	92690	GCAAATAAACCGAGTG	13	AS	811
1533325	87411	87426	89477	89492	TACCAGCTTATTGGCT	35	AS	812
1533397	22330	22345	24396	24411	GCCTATGCTTGAAGGG	25	AS	813
1533425	29771	29786	31837	31852	AGTTAGAGTGTAGTTG	27	AS	814
1533461	63401	63416	65467	65482	GTTACATAAGATCGAT	36	AS	815
1533481	40238	40253	42304	42319	GATACAAGGTGTACCA	8	AS	816
1533495	110633	110648	112699	112714	GGTACATCGAAGACAA	35	AS	817
1533497	38806	38821	40872	40887	ATTAGAACGAGGATGG	18	AS	818
1533509	129740	129755	N/A	N/A	GGCTAATCTGATGTGT	126	AS	819
1533515	74683	74698	76749	76764	AGCGAAAAGCATGGGC	15	AS	820
1533535	67785	67800	69851	69866	TGCTACGACACAGTAG	103	AS	821
1533537	46979	46994	49045	49060	AACCGTATCACTATGG	10	AS	822
1533545	120085	120100	N/A	N/A	GTACCTATCTATTCCG	100	AS	823
1533555	41632	41647	43698	43713	GAATAGCCTTTGTAGG	23	AS	824
1533557	25206	25221	27272	27287	TCAGATTAGGCCTCGG	8	AS	825
1533573	27153	27168	29219	29234	ATAGATAGACTCCTAC	36	AS	826
1533585	15095	15110	17161	17176	GCATAAGAAACGGTTG	31	AS	827

1533603	10098	10113	12164	12179	GACATAAGTCTCAAGC	108	AS	828
1533631	37007	37022	39073	39088	TAACCCGGTCTAAACC	54	AS	829
1533647	14918	14933	16984	16999	GATACGGTCATTCAGT	31	AS	830
1533687	52053	52068	54119	54134	ACCAATGGTTTGCCCC	19	AS	831
1533721	80818	80833	82884	82899	ATGGTTCGATAATAGC	16	AS	832
1533725	103450	103465	105516	105531	AATGATACACGCTGCT	56	AS	833
1533737	25855	25870	27921	27936	TCTTAGACATGCGACT	20	AS	834
1533741	85165	85180	87231	87246	CTGTTTACGGAACATG	21	AS	835
1533743	43466	43481	45532	45547	TACGGAGATATAGACT	21	AS	836
1533751	97030	97045	99096	99111	AGCCTATAATGACCCA	23	AS	837
1533759	125145	125160	N/A	N/A	GGTCATAAAGTGCAGT	95	AS	838
1533793	36270	36285	38336	38351	GCGAAGGACTATATAA	28	AS	839
1533805	19047	19062	21113	21128	AAAACCGGTGCCATTA	40	AS	840
1533827	131289	131304	N/A	N/A	ATTATTGGCCCAGTTG	89	AS	841
1533835	33218	33233	35284	35299	AACTGGAGACGGCCAC	22	AS	842
1533845	25160	25175	27226	27241	AAATATGGCGGACAGA	19	AS	843
1533873	71607	71622	73673	73688	GTCTTAAACTTAGAAC	19	AS	844
1533883	121952	121967	N/A	N/A	CGTAATCAGTAAGGAA	93	AS	845
1533905	20978	20993	23044	23059	TAGAACCTTACAGGAT	60	AS	846
1533909	17895	17910	19961	19976	AGCCCGTGAAAAGGGT	68	AS	847
1533919	26496	26511	28562	28577	CGGAATATTGTAATTA	3	AS	848
1533987	30904	30919	32970	32985	ACGAAGACAACCCTCT	34	AS	849
1534001	108847	108862	110913	110928	AACATTGCGGCAACAT	63	AS	850
1534003	5240	5255	7306	7321	GTAATTATTCCGTTGG	9	AS	851
1534005	28093	28108	30159	30174	GTATCGAAAAGTTGGC	7	AS	852
1534007	38222	38237	40288	40303	ACTATAAGGCATTGCG	38	AS	853
1534011	134483	134498	N/A	N/A	TAGGCCTAGCAGGCTC	91	AS	854
1534039	112415	112430	114481	114496	ATTCCGAGTGTAGGGT	20	AS	855
1534073	7413	7428	9479	9494	TAACCTCCTATACGGA	58	AS	856
1534083	28173	28188	30239	30254	GAAGTAAACGGGCAGC	7	AS	857
1534101	86526	86541	88592	88607	ATCCGATATTGGAATA	47	AS	858
1534135	3335	3350	5401	5416	GATTAGTAGCAGCCCT	42	AS	859
1534137	101685	101700	103751	103766	TATAGAGTGACAGGTC	25	AS	860
1482308	33281	33296	35347	35362	ACGAAGCAAAGTTGTCC	5	AT	861
1482599	38644	38659	40710	40725	ACTACCGCTGCACAGG	20	AT	862
1482902	14920	14935	16986	17001	GAGATACGGTCATTCA	38	AT	863
1483279	19868	19883	21934	21949	GATATGATAACGAAGC	13	AT	864
1483319	21471	21486	23537	23552	GCATATGTTGTGGGAT	2	AT	865
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	5	AT	168
1532944	40239	40254	42305	42320	GGATACAAGGTGTACC	11	AT	866
1532973	47898	47913	49964	49979	AACGATTTGTGTGCTA	9	AT	867
1532983	32832	32847	34898	34913	TCGCATTATCATGGTT	20	AT	868
1532999	31664	31679	33730	33745	CACTAGACGAATGCAA	13	AT	869
1533049	125292	125307	N/A	N/A	TCAATTTACTTAGCGG	96	AT	870
1533061	5241	5256	7307	7322	AGTAATTATTCCGTTG	22	AT	871

1533077	53497	53512	55563	55578	CGGTACTTATGAAGCA	7	AT	872
1533093	68233	68248	70299	70314	CATTTATGGTGTCTCG	23	AT	873
1533099	55508	55523	57574	57589	ATATTTTGTACGGATC	21	AT	874
1533129	81789	81804	83855	83870	GGTATATAGTACCAGG	11	AT	875
1533137	7414	7429	9480	9495	ATAACTTCCTATACGG	39	AT	876
1533149	101699	101714	103765	103780	AGGCATAAGTCTTGTA	28	AT	877
1533165	74695	74710	76761	76776	GAGTACAATAATAGCG	10	AT	878
1533229	117613	117628	N/A	N/A	GCTGTACTAGTACTAC	67	AT	879
1533233	30905	30920	32971	32986	TACGAAGACAACCCTC	20	AT	880
1533235	42350	42365	44416	44431	AAGCAGAGATTAGTCG	10	AT	881
1533239	134490	134505	N/A	N/A	GAGACTATAGGCCTAG	99	AT	882
1533247	37009	37024	39075	39090	CCTAACCCGGTCTAAA	56	AT	883
1533281	43477	43492	45543	45558	GTTCAAATATATACGG	6	AT	884
1533287	15678	15693	17744	17759	TTCAAGTTTAACGATC	40	AT	885
1533293	36271	36286	38337	38352	AGCGAAGGACTATATA	21	AT	886
1533323	39409	39424	41475	41490	AGAACCGGGTGAATTT	11	AT	887
1533347	38807	38822	40873	40888	CATTAGAACGAGGATG	25	AT	888
1533349	10982	10997	13048	13063	TGTTTAATGCTTTCCG	5	AT	889
1533361	115076	115091	117142	117157	CACTCAATATTTCCGG	59	AT	890
1533389	22611	22626	24677	24692	TATACGAGTTGACAAA	18	AT	891
1533403	109221	109236	111287	111302	CGTAATGAGCATGTAG	22	AT	892
1533445	15096	15111	17162	17177	AGCATAAGAAACGGTT	28	AT	893
1533517	27569	27584	29635	29650	CAATGAGTAAGGCCTC	15	AT	894
1533523	97031	97046	99097	99112	TAGCCTATAATGACCC	25	AT	895
1533547	121977	121992	N/A	N/A	CCATTGTAATGTGAGG	94	AT	896
1533593	93055	93070	95121	95136	GTAGATAATGCCCTA	20	AT	897
1533597	112416	112431	114482	114497	AATTCCGAGTGTAGGG	32	AT	898
1533625	76610	76625	78676	78691	GTCTATACATTTGGGC	29	AT	899
1533641	25207	25222	27273	27288	CTCAGATTAGGCCTCG	11	AT	900
1533645	132715	132730	N/A	N/A	TATGTTAGGACTGACG	105	AT	901
1533675	52371	52386	54437	54452	CGACATACATCTCCAA	7	AT	902
1533695	105217	105232	107283	107298	CGCAATTTTCAGGTGTC	14	AT	903
1533701	110884	110899	112950	112965	CTAAGCTTGAGTCATA	82	AT	904
1533703	24419	24434	26485	26500	CTCCATGGGTTTGGCG	24	AT	905
1533717	132266	132281	N/A	N/A	ATCAATCCAGTATGTC	65	AT	906
1533755	127312	127327	N/A	N/A	TTGGATTAGTGTCTAG	120	AT	907
1533767	28761	28776	30827	30842	GAACATACCCTACACC	70	AT	908
1533783	46344	46359	48410	48425	GGTCATTAGGGCCATC	14	AT	909
1533789	118588	118603	N/A	N/A	CGTTCTAGAGGCTCAT	64	AT	910
1533801	72557	72572	74623	74638	AAGTGTTAAGCACACG	19	AT	911
1533849	120212	120227	N/A	N/A	CGTTTGTACAGATCAT	88	AT	912
1533859	129783	129798	N/A	N/A	AGGTAAGCTAACAGTT	111	AT	913
1533887	30973	30988	33039	33054	CCACACCCGAAATACC	21	AT	914
1533891	86527	86542	88593	88608	CATCCGATATTGGAAT	36	AT	915
1533899	28095	28110	30161	30176	AAGTATCGAAAAGTTG	11	AT	916

1533901	89100	89115	91166	91181	AGTGTAACAGCTAGGG	8	AT	917
1533913	29772	29787	31838	31853	TAGTTAGAGTGTAGTT	42	AT	918
1533933	48462	48477	50528	50543	CAGCGGTAAGTTTTCC	8	AT	919
1533965	63415	63430	65481	65496	GATGTATTGTATGGGT	3	AT	920
1533975	18621	18636	20687	20702	CTAGTAGAGCTTCCTC	18	AT	921
1533977	126148	126163	N/A	N/A	CCCTTGAGAGATTGTC	97	AT	922
1533985	25161	25176	27227	27242	GAAATATGGCGGACAG	8	AT	923
1533996	71648	71663	73714	73729	TAAACGGTGCAGGACA	15	AT	924
1534021	25857	25872	27923	27938	ATTCTTAGACATGCGA	5	AT	925
1534063	44425	44440	46491	46506	CCTACAGTAGAAGTGC	26	AT	926
1534069	26497	26512	28563	28578	GCGGAATATTGTAATT	6	AT	927
1534070	28175	28190	30241	30256	TAGAAGTAAACGGGCA	15	AT	928
1534078	107051	107066	109117	109132	CGGAAC TAAGACTGAT	19	AT	929
1534103	19048	19063	21114	21129	GAAAACCGGTGCCATT	47	AT	930
1534113	3336	3351	5402	5417	AGATTAGTAGCAGCCC	21	AT	931
1534115	23626	23641	25692	25707	TTAAACCACGAGCCGT	28	AT	932
1534119	19612	19627	21678	21693	ACGCATAGTAGCATT	7	AT	933
1534123	17899	17914	19965	19980	TATTAGCCCGTGAAAA	63	AT	934
1534145	43963	43978	46029	46044	TTCGCTAGGAGAAACA	15	AT	935
1534161	34059	34074	36125	36140	GAAAGTTTCACGCTAA	16	AT	936
1534167	85399	85414	87465	87480	TACGAGTTTGTCTGTC	17	AT	937

The modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 3 (GENBANK Accession No: NM_001146055.1), as indicated. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

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Table 2

3-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 3 Start Site	SEQ ID NO: 3 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1482273	41	56	TTTACACCACACTCTT	76	B	938

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 1,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC).

“Start site” indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. “Stop site” indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100%

complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

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Table 3

3-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1482214	40517	40532	42583	42598	GTGAATAATTCTGTAC	31	C	939
1482455	48872	48887	50938	50953	AGAGGAAGGTAAAGGT	35	C	940
1483179	33904	33919	35970	35985	TGACTATCAGTATCTG	27	C	941
1483250	21431	21446	23497	23512	ACTGATCCTAAGATTT	37	C	942
1483668	2649	2664	4715	4730	TCATGAATACATCCAT	28	C	943
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	15	C	19
1483996	19320	19335	21386	21401	GAGTTAATATTGTTCT	15	C	944
1484504	78723	78738	80789	80804	AGGAATTAACCATCAT	18	C	945
1484515	25075	25090	27141	27156	ACGTTTAGACCATATG	14	C	946
1484519	72235	72250	74301	74316	TGTGAATAGAACTCTG	22	C	947
1484635	35371	35386	37437	37452	TGGAATAATTGTACTG	9	C	948
1484641	14834	14849	16900	16915	GAAGTTTAATTTTCATG	34	C	949
1484649	87051	87066	89117	89132	TCAATATAATGAATCC	32	C	950
1484672	48011	48026	50077	50092	ATTCAGTATCTTCAGC	39	C	951
1484687	48749	48764	50815	50830	ACATAGTTATCTAGGA	23	C	952
1484733	36900	36915	38966	38981	AGTACATATCAAAGTA	17	C	953
1484775	87629	87644	89695	89710	ACAACTATCACTTGTC	54	C	954
1484815	18183	18198	20249	20264	CTAGTTGTCCATAACT	55	C	955
1484827	36370	36385	38436	38451	TACAATCTACACAGGC	14	C	956
1484839	45450	45465	47516	47531	ACACATTATTTGCCTA	26	C	957
1484870	21129	21144	23195	23210	ACCCATATGTTACTCA	11	C	958
1484873	41663	41678	43729	43744	ATATTGTAACCCCCTT	48	C	959
1484962	44570	44585	46636	46651	AATGTTATTCTACCAC	50	C	960
1484999	33475	33490	35541	35556	CTGTACAACCTAACCAC	53	C	961
1485051	15586	15601	17652	17667	AGTTATATTTGAACCA	52	C	962
1485104	27291	27306	29357	29372	ATGTACTATAACCAGA	16	C	963
1485105	30207	30222	32273	32288	ATTTATCTCATGAGTG	19	C	964
1485157	39382	39397	41448	41463	TGATACAACCTTATCA	37	C	965
1485186	28999	29014	31065	31080	TTTGTAACCTAATCTGG	15	C	966
1485188	94847	94862	96913	96928	CATGTTAACATGAGTC	36	C	967
1485246	26066	26081	28132	28147	TCACATACTGCAACAA	15	C	968
1485379	20302	20317	22368	22383	TCCATAACACTCAAGT	35	C	969
1485393	25761	25776	27827	27842	CTAACCATATTGTTCT	25	C	970

1485516	16722	16737	18788	18803	GAAACTTCAACGTTGT	24	C	971
1485620	38360	38375	40426	40441	TAAACTGAGACCTGTT	49	C	972
1485624	43683	43698	45749	45764	TATCATCAAGTCATGG	10	C	973
1485639	41200	41215	43266	43281	CCATGAAGGTACACCT	40	C	974
1485679	23366	23381	25432	25447	ATCTATCTATGCTTTG	24	C	975
1485708	64426	64441	66492	66507	CACACTTAGTCATTCT	27	C	976
1485720	38886	38901	40952	40967	GATAGATACTGAATTT	21	C	977
1485778	44961	44976	47027	47042	CATATTAATTGTTACC	10	C	978
1485788	29899	29914	31965	31980	GACAATGTCATTTATC	34	C	979
1485806	31420	31435	33486	33501	GTATTAATTTCAAGCT	17	C	980
1485809	24426	24441	26492	26507	AACTATTCTCCATGGG	26	C	981
1485824	23839	23854	25905	25920	TTCAAGCTATTAAACA	31	C	982
1485869	19652	19667	21718	21733	CTGGGATAGACCAAGT	14	C	983
1485870	22413	22428	24479	24494	GAACCAAAAGACCTCT	15	C	984
1485872	85849	85864	87915	87930	CACCAATATTCCCCAA	33	C	985
1485965	46176	46191	48242	48257	TCATAGCCAATCCCCT	42	C	986
1485979	18657	18672	20723	20738	CAGAACTTTATTGCTA	23	C	987
1485997	71852	71867	73918	73933	ACCTTAAACTCCAAGT	24	C	988
1486001	40155	40170	42221	42236	TGCAATAGTTACATGT	59	C	989
1486046	32722	32737	34788	34803	CTATTACTTTAGCTTT	19	C	990
1486055	47361	47376	49427	49442	TGTTATATGACAATGC	22	C	991
1486064	50069	50084	52135	52150	ACTGATAGAACACTGC	21	C	992
1486086	71172	71187	73238	73253	AATCAATGAACACTTG	38	C	993
1486106	70751	70766	72817	72832	TATCCTTAGATCTACA	38	C	994
1486132	22977	22992	25043	25058	GAATTCATTCCTATGA	33	C	995
1486158	43133	43148	45199	45214	TTTATGTCAAACCCGG	16	C	996
1486178	27823	27838	29889	29904	GCATTTGGCCCTCTGG	24	C	997
1486188	37355	37370	39421	39436	GCTACATCAATGCACT	18	C	998
1486231	86325	86340	88391	88406	AAAGAACAATTGTACC	83	C	999
1486241	20733	20748	22799	22814	TGCTTTAATCTAAGAT	27	C	1000
1486243	17635	17650	19701	19716	ATCATTAGCATCCATT	25	C	1001
1486249	46435	46450	48501	48516	TTAGAGTAACACATCC	17	C	1002
1486271	16108	16123	18174	18189	GAACCGTAATCTCACC	23	C	1003
1486275	21786	21801	23852	23867	TCTCATTAATGAAACC	21	C	1004
1486309	102648	102663	104714	104729	TCTATTATCAATTCCT	44	C	1005
1486392	33025	33040	35091	35106	CGCATAGAGAATTCCT	28	C	1006
1486468	34966	34981	37032	37047	ACCTAAGTTTTCTCCA	17	C	1007
1486484	37873	37888	39939	39954	TTTACATAACCAGACT	57	C	1008
1486528	39801	39816	41867	41882	ACAACATTAAATAGTC	29	C	1009
1486535	44044	44059	46110	46125	CATCCTTAACCTCAAT	31	C	1010
1486578	30968	30983	33034	33049	CCCGAAATACCACCTG	29	C	1011
1486582	32009	32024	34075	34090	GAAGAGTTAATATCAG	47	C	1012
1486592	28362	28377	30428	30443	GAACCTAGACATTTGG	9	C	1013

1486689	26484	26499	28550	28565	ATTACCATTTATGTTG	32	C	1014
1482380	2650	2665	4716	4731	TTCATGAATACATCCA	32	D	1015
1482386	2620	2635	4686	4701	CTTTACACCACACTGG	39	D	1016
1482848	48874	48889	50940	50955	TAAGAGGAAGGTAAAG	65	D	1017
1483031	32723	32738	34789	34804	GCTATTACTTTAGCTT	87	D	1018
1483553	43686	43701	45752	45767	AAGTATCATCAAGTCA	19	D	1019
1483741	33498	33513	35564	35579	GAGTTTACAATTTGGC	12	D	1020
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	16	D	19
1484338	29969	29984	32035	32050	TTAACACATTCTTGCA	52	D	1021
1484490	45473	45488	47539	47554	GAACATTGGCCTAAGT	30	D	1022
1484531	22991	23006	25057	25072	TCCATAATGTAAGTGA	24	D	1023
1484544	35430	35445	37496	37511	TGGTATAAGCCATCAC	26	D	1024
1484571	39386	39401	41452	41467	TATTTGATACAACCTTA	36	D	1025
1484579	26511	26526	28577	28592	AAGTTTTAACCAGTGC	12	D	1026
1484603	71853	71868	73919	73934	CACCTTAAACTCCAAG	41	D	1027
1484705	38890	38905	40956	40971	ACATGATAGATACTGA	26	D	1028
1484760	23377	23392	25443	25458	GAAGTATTTCTATCTA	28	D	1029
1484776	23847	23862	25913	25928	TCTTAAGATTCAAGCT	28	D	1030
1484821	44962	44977	47028	47043	GCATATTAATTGTTAC	28	D	1031
1484853	40518	40533	42584	42599	CGTGAATAATTCTGTA	28	D	1032
1484869	36903	36918	38969	38984	GTAAGTACATATCAAA	29	D	1033
1484928	44643	44658	46709	46724	CCTGTTTAAAAGTAGG	78	D	1034
1484948	27890	27905	29956	29971	GTAACATTATGAAAGG	22	D	1035
1484968	25076	25091	27142	27157	CACGTTTAGACCATAT	34	D	1036
1484984	87630	87645	89696	89711	GACAACATCACTTGT	64	D	1037
1485050	37356	37371	39422	39437	TGCTACATCAATGCAC	72	D	1038
1485052	71187	71202	73253	73268	CATAATCCACCTCTGA	47	D	1039
1485060	30208	30223	32274	32289	GATTTATCTCATGAGT	7	D	1040
1485064	72285	72300	74351	74366	CAAAGGACCTTTCTTC	50	D	1041
1485115	26135	26150	28201	28216	TAAGCCACATACAGGT	27	D	1042
1485116	86349	86364	88415	88430	TGTTATCTTAAGAGGC	21	D	1043
1485137	102809	102824	104875	104890	CTACTTCTCTACCTCA	42	D	1044
1485147	41303	41318	43369	43384	GAAATCATATATCTTC	37	D	1045
1485190	39808	39823	41874	41889	CCATCAAACAACATTA	49	D	1046
1485211	37874	37889	39940	39955	TTTTACATAACCAGAC	45	D	1047
1485245	48750	48765	50816	50831	AACATAGTTATCTAGG	21	D	1048
1485252	19331	19346	21397	21412	ACTAAACACAAGAGTT	41	D	1049
1485310	46178	46193	48244	48259	TCTCATAGCCAATCCC	35	D	1050
1485330	87116	87131	89182	89197	CTTCATAAATGATGG	42	D	1051
1485342	64568	64583	66634	66649	GAGGTTATAACGTGAG	25	D	1052
1485373	21437	21452	23503	23518	TTAACCACTGATCCTA	48	D	1053
1485413	21130	21145	23196	23211	CACCCATATGTTACTC	25	D	1054
1485439	48017	48032	50083	50098	GTTATTATTCAGTATC	30	D	1055

1485450	29019	29034	31085	31100	GCAAAACCACTGGCTA	33	D	1056
1485474	16723	16738	18789	18804	TGAAACTTCAACGTTG	37	D	1057
1485498	47364	47379	49430	49445	CTATGTTATATGACAA	42	D	1058
1485500	70758	70773	72824	72839	TACTTTGTATCCTTAG	44	D	1059
1485504	22414	22429	24480	24495	AGAACCAAAAGACCTC	16	D	1060
1485549	30970	30985	33036	33051	CACCCGAAATACCACC	40	D	1061
1485596	15587	15602	17653	17668	CAGTTATATTTGAACC	30	D	1062
1485681	50187	50202	52253	52268	GCGTATCTTTTCCAG	35	D	1063
1485718	18672	18687	20738	20753	ATTATTATAGAACTC	40	D	1064
1485830	40175	40190	42241	42256	ACCTTACTACATGCAA	40	D	1065
1485851	33026	33041	35092	35107	TCGCATAGAGAATTCC	32	D	1066
1485894	28363	28378	30429	30444	TGAACCTAGACATTG	38	D	1067
1485938	25762	25777	27828	27843	TCTAACCATATTGTC	46	D	1068
1485992	33906	33921	35972	35987	AATGACTATCAGTATC	51	D	1069
1486022	36375	36390	38441	38456	GAATTTACAATCTACA	55	D	1070
1486040	20734	20749	22800	22815	ATGCTTTAATCTAAGA	31	D	1071
1486108	44047	44062	46113	46128	CATCATCCTTAAC TTC	48	D	1072
1486114	79253	79268	81319	81334	TATCGTAAGGTCAAGT	42	D	1073
1486161	41664	41679	43730	43745	AATATTGTAACCCCT	60	D	1074
1486212	14837	14852	16903	16918	GCAGAAGTTTAATTC	44	D	1075
1486213	21798	21813	23864	23879	CATTTAACAGTATCTC	19	D	1076
1486222	19674	19689	21740	21755	CAAGCAAGACACTGTT	19	D	1077
1486229	32025	32040	34091	34106	GAAACAATGCATCTTA	36	D	1078
1486244	17636	17651	19702	19717	CATCATTAGCATCCAT	26	D	1079
1486272	27292	27307	29358	29373	AATGTACTATAACCAG	23	D	1080
1486303	38362	38377	40428	40443	GTAAACTGAGACCTG	37	D	1081
1486403	85866	85881	87932	87947	GCAATAAAAACCATGC	54	D	1082
1486407	43136	43151	45202	45217	AAATTTATGTCAAACC	52	D	1083
1486409	34967	34982	37033	37048	TACCTAAGTTTTCTCC	26	D	1084
1486424	31421	31436	33487	33502	GGTATTAATTTCAAGC	11	D	1085
1486436	24427	24442	26493	26508	GAACTATTCTCCATGG	28	D	1086
1486464	95265	95280	97331	97346	TATTTTATGCTTCAGG	40	D	1087
1486485	16118	16133	18184	18199	ACATGAAAATGAACCG	20	D	1088
1486619	20303	20318	22369	22384	GTCCATAACACTCAAG	23	D	1089
1486663	46448	46463	48514	48529	ATCTTAGAGATCCTTA	44	D	1090
1486679	18192	18207	20258	20273	TAGTTAAATCTAGTTG	52	D	1091
1482724	37875	37890	39941	39956	GTTTTACATAACCAGA	37	E	1092
1483232	2651	2666	4717	4732	TTTCATGAATACATCC	19	E	1093
1483775	43687	43702	45753	45768	GAAGTATCATCAAGTC	6	E	1094
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	15	E	19
1483947	2621	2636	4687	4702	CCTTTACACCACACTG	40	E	1095
1483954	40531	40546	42597	42612	AGAGTAATGCTATCGT	18	E	1096
1484164	48875	48890	50941	50956	TTAAGAGGAAGGTAAA	69	E	1097

1484498	48752	48767	50818	50833	AGAACATAGTTATCTA	51	E	1098
1484503	85905	85920	87971	87986	TAGGTATTCAGATGTT	26	E	1099
1484526	44751	44766	46817	46832	ATCCAAATTGCCTTTT	42	E	1100
1484580	16807	16822	18873	18888	CTTGATTTATTCAAGA	71	E	1101
1484623	27342	27357	29408	29423	GGATATCCAAAATGGT	61	E	1102
1484744	36904	36919	38970	38985	TGTAAGTACATATCAA	36	E	1103
1484745	72286	72301	74352	74367	GCAAAGGACCTTTCTT	41	E	1104
1484789	87644	87659	89710	89725	AAGTTAACTCCCTTGA	53	E	1105
1484856	79576	79591	81642	81657	AGATCATCATAGTTGC	13	E	1106
1484859	26137	26152	28203	28218	CATAAGCCACATACAG	47	E	1107
1484949	15588	15603	17654	17669	GCAGTTATATTTGAAC	48	E	1108
1484952	32048	32063	34114	34129	GAAATCAGACAATGGT	7	E	1109
1485013	44964	44979	47030	47045	GTGCATATTAATTGTT	10	E	1110
1485018	18697	18712	20763	20778	AGACATTTATTAGAGT	9	E	1111
1485021	19333	19348	21399	21414	GTACTAAACACAAGAG	33	E	1112
1485131	33039	33054	35105	35120	CATAGAGATCCTCTCG	34	E	1113
1485148	36376	36391	38442	38457	AGAATTTACAATCTAC	40	E	1114
1485199	27931	27946	29997	30012	GTAATAAAGTCACGGG	14	E	1115
1485200	103053	103068	105119	105134	TTATTGAACAATGTCA	53	E	1116
1485223	38896	38911	40962	40977	GAATTCACATGATAGA	25	E	1117
1485235	33908	33923	35974	35989	CTAATGACTATCAGTA	26	E	1118
1485263	50626	50641	52692	52707	GCTACTTCGAAGTGGG	24	E	1119
1485278	38364	38379	40430	40445	AAGTTAACTGAGACC	23	E	1120
1485364	25101	25116	27167	27182	GAAGTATTAGAGAGGA	15	E	1121
1485368	21183	21198	23249	23264	GGTAAATATGTCAGTC	16	E	1122
1485392	28365	28380	30431	30446	TGTGAACCTAGACATT	32	E	1123
1485412	23848	23863	25914	25929	GTCTTAAGATTCAAGC	13	E	1124
1485415	45479	45494	47545	47560	TACGTTGAACATTGGC	13	E	1125
1485455	95266	95281	97332	97347	GTATTTTATGCTTCAG	20	E	1126
1485540	22992	23007	25058	25073	ATCCATAATGTAAC TG	12	E	1127
1485552	18193	18208	20259	20274	CTAGTTAAATCTAGTT	50	E	1128
1485560	23414	23429	25480	25495	CTACTTTAGATATGTC	12	E	1129
1485605	40176	40191	42242	42257	AACCTTACTACATGCA	22	E	1130
1485618	22416	22431	24482	24497	TGAGAACCAAAAGACC	19	E	1131
1485630	70782	70797	72848	72863	TTTTAGTTCCTCCTAC	72	E	1132
1485640	46450	46465	48516	48531	GAATCTTAGAGATCCT	25	E	1133
1485667	19698	19713	21764	21779	AAGGATTTATTTGAGC	39	E	1134
1485728	16151	16166	18217	18232	ACAGTAAGTATCTTGC	15	E	1135
1485748	24428	24443	26494	26509	AGAACTATTCTCCATG	22	E	1136
1485781	41318	41333	43384	43399	GACCACCACAATTGAG	32	E	1137
1485803	39438	39453	41504	41519	TTCTAGCCACCACATT	36	E	1138
1485804	17696	17711	19762	19777	ACCAACCATGCATTCA	32	E	1139
1485860	48018	48033	50084	50099	GGTTATTATTCAGTAT	13	E	1140

1485880	47414	47429	49480	49495	GAAATTTTCCAGCTAT	17	E	1141
1485891	71188	71203	73254	73269	TCATAATCCACCTCTG	65	E	1142
1485953	26512	26527	28578	28593	TAAGTTTTAACCAGTG	14	E	1143
1486000	34969	34984	37035	37050	CGTACCTAAGTTTTCT	28	E	1144
1486090	37370	37385	39436	39451	TGGATTAGAACCACTG	23	E	1145
1486107	29080	29095	31146	31161	CCAGATAAAACAAGGC	36	E	1146
1486123	20318	20333	22384	22399	TCATTTAATCAGAGGG	31	E	1147
1486138	30971	30986	33037	33052	ACACCCGAAATACCAC	31	E	1148
1486146	21438	21453	23504	23519	ATTAACCACTGATCCT	46	E	1149
1486175	35431	35446	37497	37512	CTGGTATAAGCCATCA	27	E	1150
1486200	20738	20753	22804	22819	CAGTATGCTTTAATCT	17	E	1151
1486220	33520	33535	35586	35601	ATGTAACGTCACATTA	27	E	1152
1486276	46185	46200	48251	48266	TATGTATTCTCATAGC	22	E	1153
1486348	30209	30224	32275	32290	AGATTTATCTCATGAG	8	E	1154
1486372	32724	32739	34790	34805	AGCTATTACTTTAGCT	64	E	1155
1486433	29970	29985	32036	32051	TTTAACACATTCTTGC	17	E	1156
1486444	21800	21815	23866	23881	TACATTTAACAGTATC	36	E	1157
1486458	15022	15037	17088	17103	AAGCTAAATTTGCAGT	60	E	1158
1486462	44054	44069	46120	46135	GAGGAGACATCATCCT	90	E	1159
1486467	86350	86365	88416	88431	CTGTTATCTTAAGAGG	28	E	1160
1486531	41667	41682	43733	43748	GCAAATATTGTAACCC	12	E	1161
1486559	87159	87174	89225	89240	TACAATCTGTAACTG	27	E	1162
1486566	43243	43258	45309	45324	GATACTCAATCTCTTA	14	E	1163
1486574	71854	71869	73920	73935	TCACCTTAAACTCCAA	30	E	1164
1486623	65100	65115	67166	67181	ACTTATCAGTCATTCA	34	E	1165
1486626	31422	31437	33488	33503	AGGTATTAATTTCAAG	15	E	1166
1486662	25763	25778	27829	27844	CTCTAACCATATTGTT	54	E	1167
1486694	39810	39825	41876	41891	TACCATCAAACAACAT	29	E	1168
1482187	39442	39457	41508	41523	AATTTTCTAGCCACCA	28	F	1169
1482723	48020	48035	50086	50101	GAGGTTATTATTCAGT	16	F	1170
1482930	33909	33924	35975	35990	ACTAATGACTATCAGT	55	F	1171
1482944	19334	19349	21400	21415	TGTACTAAACACAAGA	42	F	1172
1483106	37876	37891	39942	39957	TGTTTTACATAACCAG	11	F	1173
1483293	25770	25785	27836	27851	GTTTATTCTCTAACCA	16	F	1174
1483347	70785	70800	72851	72866	GCTTTTTAGTTCCTCC	15	F	1175
1483368	48835	48850	50901	50916	TATTATTAAATTGGGC	45	F	1176
1483486	48876	48891	50942	50957	ATTAAGAGGAAGGTAA	43	F	1177
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	16	F	19
1484059	2652	2667	4718	4733	CTTTCATGAATACATC	36	F	1178
1484497	30987	31002	33053	33068	ACTATAAAGATCTGCC	50	F	1179
1484507	21802	21817	23868	23883	CCTACATTTAACAGTA	51	F	1180
1484625	23849	23864	25915	25930	TGTCTTAAGATTCAAG	22	F	1181
1484674	41323	41338	43389	43404	GTAACGACCACCACAA	23	F	1182

1484679	25115	25130	27181	27196	CCTTTTAGACCCCTGA	34	F	1183
1484707	22454	22469	24520	24535	ACATATTTTGTCTGA	7	F	1184
1484757	33040	33055	35106	35121	GCATAGAGATCCTCTC	9	F	1185
1484758	43246	43261	45312	45327	AAGGATACTCAATCTC	25	F	1186
1484772	21185	21200	23251	23266	AGGGTAAATATGTCAG	15	F	1187
1484826	46188	46203	48254	48269	GCTTATGTATTCTCAT	17	F	1188
1484840	29140	29155	31206	31221	CTACCTAGAATGAAGA	54	F	1189
1484953	23415	23430	25481	25496	CCTACTTTAGATATGT	20	F	1190
1484972	46469	46484	48535	48550	GCAATTTAACAACCTGC	53	F	1191
1485006	87645	87660	89711	89726	GAAGTTAACTCCCTTG	31	F	1192
1485010	36379	36394	38445	38460	GGAAGAATTTACAATC	19	F	1193
1485036	29971	29986	32037	32052	GTTTAACACATTCTTG	25	F	1194
1485094	87164	87179	89230	89245	AGTAGTACAATCTGTT	26	F	1195
1485108	43688	43703	45754	45769	AGAAGTATCATCAAGT	10	F	1196
1485118	24429	24444	26495	26510	TAGAACTATTCTCCAT	34	F	1197
1485119	36905	36920	38971	38986	ATGTAAGTACATATCA	21	F	1198
1485130	65281	65296	67347	67362	CATATTCACATCAATCCA	33	F	1199
1485140	15660	15675	17726	17741	GAATGTAAAGCCATGA	26	F	1200
1485210	26523	26538	28589	28604	GCTTATTTACATAAGT	62	F	1201
1485213	85917	85932	87983	87998	GCATTAACCTCAATAGG	10	F	1202
1485239	27351	27366	29417	29432	ACCAATACTGGATATC	73	F	1203
1485255	30212	30227	32278	32293	TCAAGATTTATCTCAT	29	F	1204
1485257	20319	20334	22385	22400	ATCATTTAATCAGAGG	13	F	1205
1485271	34970	34985	37036	37051	ACGTACCTAAGTTTTTC	34	F	1206
1485347	21439	21454	23505	23520	TATTAACCACTGATCC	56	F	1207
1485408	38897	38912	40963	40978	AGAATTCACATGATAG	20	F	1208
1485419	28389	28404	30455	30470	CCAAAGATATAACTTA	37	F	1209
1485436	47415	47430	49481	49496	TGAAATTTTCCAGCTA	33	F	1210
	78926	78941	80992	81007				
1485541	33521	33536	35587	35602	AATGTAACGTCACATT	58	F	1211
1485555	32725	32740	34791	34806	TAGCTATTACTTTAGC	47	F	1212
1485573	16830	16845	18896	18911	GAACGTGTCAGGGCAA	10	F	1213
1485579	18730	18745	20796	20811	TTTTTAGCATCCCATA	30	F	1214
1485671	31452	31467	33518	33533	GCATATAACCAAATTC	10	F	1215
1485695	37371	37386	39437	39452	CTGGATTAGAACCACT	40	F	1216
1485736	50892	50907	52958	52973	AAATTTCTATACTCCC	28	F	1217
1485759	39813	39828	41879	41894	ATGTACCATCAAACAA	26	F	1218
1485784	26138	26153	28204	28219	ACATAAGCCACATACA	28	F	1219
1485801	45009	45024	47075	47090	CTCAATCAACATAGGT	20	F	1220
1485811	95658	95673	97724	97739	GCAGATAAGCCATTTT	27	F	1221
1485814	41696	41711	43762	43777	CCCTTTACAGATCCAA	21	F	1222
1485843	18196	18211	20262	20277	CCTCTAGTTAAATCTA	22	F	1223
1485951	38408	38423	40474	40489	GGTGATAACTGATATG	18	F	1224

1485973	16196	16211	18262	18277	AAGGTAGCACTTTTTC	10	F	1225
1485984	40540	40555	42606	42621	GAGCTATTAAGAGTAA	31	F	1226
1485998	40177	40192	42243	42258	GAACCTTACTACATGC	27	F	1227
1486021	104250	104265	106316	106331	TCATTTTCGTACTCGTC	48	F	1228
1486038	45480	45495	47546	47561	TTACGTTGAACATTGG	14	F	1229
1486048	71883	71898	73949	73964	ACATTTCCAAACCACG	24	F	1230
1486057	44753	44768	46819	46834	CTATCCAAATTGCCTT	25	F	1231
1486068	17727	17742	19793	19808	AGCATATTTTGTACAA	7	F	1232
1486094	44079	44094	46145	46160	GTAAATAGTATTTTGG	32	F	1233
1486140	71189	71204	73255	73270	CTCATAATCCACCTCT	50	F	1234
1486141	20784	20799	22850	22865	CATACCTTTAGAAACA	19	F	1235
1486215	15061	15076	17127	17142	TTTATAGAACTTCAGG	55	F	1236
1486237	32088	32103	34154	34169	AAGTATTGACTCTACT	48	F	1237
1486256	35817	35832	37883	37898	CGTAATCTCACCTAC	56	F	1238
1486450	80813	80828	82879	82894	TCGATAATAGCTAAGC	26	F	1239
1486524	19713	19728	21779	21794	GCTCATTAGTTCAGCA	86	F	1240
1486530	27932	27947	29998	30013	GGTAATAAAGTCACGG	5	F	1241
1486541	72306	72321	74372	74387	TCCTACCATTGACTAA	55	F	1242
1486610	86358	86373	88424	88439	GCAATTATCTGTTATC	20	F	1243
1486684	22996	23011	25062	25077	CACAATCCATAATGTA	12	F	1244
1482156	80971	80986	83037	83052	TCAATTACATAGTCAG	16	G	1245
1482442	70786	70801	72852	72867	AGCTTTTTAGTTCCTC	7	G	1246
1482543	71190	71205	73256	73271	TCTCATAATCCACCTC	37	G	1247
1482546	48878	48893	50944	50959	GAATTAAGAGGAAGGT	16	G	1248
1482560	29974	29989	32040	32055	ACTGTTTAACACATTC	16	G	1249
1482588	21441	21456	23507	23522	ACTATTAACCACTGAT	79	G	1250
1482766	46189	46204	48255	48270	AGCTTATGTATTCTCA	15	G	1251
1482885	2622	2637	4688	4703	TCCTTTACACCACACT	16	G	1252
1482973	37878	37893	39944	39959	CATGTTTTACATAACC	14	G	1253
1483823	2653	2668	4719	4734	CCTTTCATGAATACAT	22	G	1254
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	10	G	19
1483846	48836	48851	50902	50917	ATATTATTAAATTGGG	43	G	1255
1483880	19846	19861	21912	21927	CTGTATTATTTGTCAG	37	G	1256
1484181	15675	15690	17741	17756	AAGTTTAACGATCAGG	26	G	1257
1484477	33538	33553	35604	35619	ATCATAGCACTATATA	25	G	1258
1484501	21804	21819	23870	23885	ATCCTACATTTAACAG	36	G	1259
1484513	24430	24445	26496	26511	CTAGAACTATTCTCCA	33	G	1260
1484539	47418	47433	49484	49499	GATTGAAATTTTCCAG	23	G	1261
1484558	22455	22470	24521	24536	AACATATTTTGTCTG	7	G	1262
1484585	23002	23017	25068	25083	ATTCATCACAATCCAT	27	G	1263
1484608	17127	17142	19193	19208	TGAATAACACTTTGGC	10	G	1264
1484644	50940	50955	53006	53021	ACTAATTCCTCTTGAG	71	G	1265
1484678	35818	35833	37884	37899	GCGTAATCTCACCTA	25	G	1266

1484725	27934	27949	30000	30015	GAGGTAATAAAGTCAC	17	G	1267
1484728	37382	37397	39448	39463	CACAATTGGCCCTGGA	37	G	1268
1484729	23416	23431	25482	25497	GCCTACTTTAGATATG	36	G	1269
1484730	15097	15112	17163	17178	CAGCATAAGAAACGGT	49	G	1270
1484769	36906	36921	38972	38987	GATGTAAGTACATATC	34	G	1271
1484811	30214	30229	32280	32295	CTTCAAGATTTATCTC	17	G	1272
1484892	19335	19350	21401	21416	ATGTACTAAACACAAG	37	G	1273
1484894	30989	31004	33055	33070	TTACTATAAAGATCTG	31	G	1274
1484910	44755	44770	46821	46836	CACTATCCAAATTGCC	15	G	1275
1484915	32728	32743	34794	34809	GGATAGCTATTACTTT	37	G	1276
1484919	17815	17830	19881	19896	AAATCTTACGAAGCTA	37	G	1277
1484937	38899	38914	40965	40980	AGAGAATTCACATGAT	15	G	1278
1485037	18731	18746	20797	20812	TTTTTTAGCATCCCAT	17	G	1279
1485062	48060	48075	50126	50141	TTTAATTACTGATTGG	12	G	1280
1485079	21186	21201	23252	23267	CAGGGTAAATATGTCA	28	G	1281
1485141	18220	18235	20286	20301	CTTAATATTCTGAAGC	25	G	1282
1485184	45487	45502	47553	47568	AATTACTTTACGTTGA	18	G	1283
1485195	20320	20335	22386	22401	AATCATTTAATCAGAG	29	G	1284
1485222	43262	43277	45328	45343	TCATATCACTTCCTGA	25	G	1285
1485285	66167	66182	68233	68248	GCATGTAAAATGCACC	32	G	1286
1485320	39443	39458	41509	41524	AAATTTTCTAGCCACC	28	G	1287
1485332	20788	20803	22854	22869	GTTACATACCTTTAGA	20	G	1288
1485360	104251	104266	106317	106332	ATCATTTTCGTA CTCTG	24	G	1289
1485377	40544	40559	42610	42625	GTTAGAGCTATTAAGA	22	G	1290
1485380	25810	25825	27876	27891	TGATAGACTTCCAACA	32	G	1291
1485411	26140	26155	28206	28221	GTACATAAGCCACATA	25	G	1292
1485441	38519	38534	40585	40600	AAAATCATCTTATGGC	26	G	1293
1485490	44163	44178	46229	46244	AGGAATATGCTATAGG	22	G	1294
1485532	95930	95945	97996	98011	GCACTACCTCTATCCA	49	G	1295
1485570	16369	16384	18435	18450	CTTACAATTAACATGA	29	G	1296
1485637	32090	32105	34156	34171	AAAAGTATTGACTCTA	29	G	1297
1485656	23858	23873	25924	25939	TGAATACATTGTCTTA	12	G	1298
1485687	27354	27369	29420	29435	GATACCAATACTGGAT	90	G	1299
1485777	71936	71951	74002	74017	TACAATTTCTGTCCTG	16	G	1300
1485779	25116	25131	27182	27197	CCCTTTTAGACCCCTG	37	G	1301
1485807	43689	43704	45755	45770	TAGAAGTATCATCAAG	18	G	1302
1485815	29142	29157	31208	31223	GTCTACCTAGAATGAA	55	G	1303
1486009	45042	45057	47108	47123	TGCCTTAAAATGATGC	30	G	1304
1486067	46470	46485	48536	48551	TGCAATTTAACA ACTG	21	G	1305
1486128	41726	41741	43792	43807	ATGTTTATCCCCCTGC	14	G	1306
1486259	86360	86375	88426	88441	TGGCAATTATCTGTTA	31	G	1307
1486267	31453	31468	33519	33534	CGCATATAACCAAATT	15	G	1308
1486277	33042	33057	35108	35123	TTGCATAGAGATCCTC	16	G	1309

1486316	41325	41340	43391	43406	ATGTAACGACCACCAC	42	G	1310
1486328	26530	26545	28596	28611	GCAGAATGCTTATTTA	31	G	1311
1486340	72438	72453	74504	74519	AAGGTTTGTACTACTT	24	G	1312
1486370	36403	36418	38469	38484	GGTGAATAAAATGTCT	24	G	1313
1486429	39817	39832	41883	41898	AATAATGTACCATCAA	33	G	1314
1486495	33910	33925	35976	35991	TACTAATGACTATCAG	24	G	1315
1486517	40180	40195	42246	42261	AATGAACCTTACTACA	42	G	1316
1486569	87166	87181	89232	89247	CAAGTAGTACAATCTG	24	G	1317
1486584	34971	34986	37037	37052	TACGTACCTAAGTTTT	39	G	1318
1486639	85960	85975	88026	88041	AGCAACCTTTTTCTCA	26	G	1319
1486651	86642	86657	88708	88723	ATGAAGTTAACTCCCT	26	G	1320
	87647	87662	89713	89728				
1486698	28390	28405	30456	30471	CCCAAAGATATAACTT	26	G	1321
1482381	33911	33926	35977	35992	GTACTAATGACTATCA	33	H	1322
1482511	70807	70822	72873	72888	ATAGTTGTCATCCTGC	27	H	1323
1483256	48844	48859	50910	50925	CTGCAATAATATTATT	89	H	1324
1483491	2623	2638	4689	4704	TTCCTTTACACCACAC	20	H	1325
1483495	71193	71208	73259	73274	ATATCTCATAATCCAC	45	H	1326
1483601	2654	2669	4720	4735	TCCTTTCATGAATACA	47	H	1327
1483765	47420	47435	49486	49501	CTGATTGAAATTTTCC	31	H	1328
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	14	H	19
1484206	19847	19862	21913	21928	GCTGTATTATTTGTCA	30	H	1329
1484237	46502	46517	48568	48583	CAAATTTCCACCATGG	66	H	1330
1484548	18253	18268	20319	20334	GGTGAATAAAAGACGG	21	H	1331
1484562	81076	81091	83142	83157	GAAACTGCTTATTTCC	60	H	1332
1484587	45488	45503	47554	47569	GAATTACTTTACGTTG	14	H	1333
1484626	25269	25284	27335	27350	CATACACCCTGATTCC	43	H	1334
1484640	27355	27370	29421	29436	GGATACCAATACTGGA	42	H	1335
1484646	30303	30318	32369	32384	CCAATTGCCATTCTAA	34	H	1336
1484654	22461	22476	24527	24542	CACGTAAACATATTTT	14	H	1337
1484668	104252	104267	106318	106333	TATCATTTTCGTA CTG	41	H	1338
1484696	48081	48096	50147	50162	CATATATTCATCAGGT	19	H	1339
1484715	36470	36485	38536	38551	CAATCAATTCTTGAGG	27	H	1340
1484885	16379	16394	18445	18460	AATTCCAAGACTTACA	35	H	1341
1484890	41326	41341	43392	43407	CATGTAACGACCACCA	27	H	1342
1484947	74042	74057	76108	76123	ATCATAAATTCCCTGC	59	H	1343
1484959	46219	46234	48285	48300	GAAACAATCTCCTTGG	29	H	1344
1484987	71938	71953	74004	74019	CATACAATTTCTGTCC	36	H	1345
1485001	86644	86659	88710	88725	AGATGAAGTTAACTCC	30	H	1346
	87649	87664	89715	89730				
1485069	66232	66247	68298	68313	TCAATACATGCACTCC	36	H	1347
1485072	29978	29993	32044	32059	CCTTACTGTTTAACAC	22	H	1348
1485088	35913	35928	37979	37994	ACTGTATCTAGACTGA	11	H	1349

1485096	24431	24446	26497	26512	CCTAGAACTATTCTCC	33	H	1350
1485102	85961	85976	88027	88042	TAGCAACCTTTTTCTC	49	H	1351
1485134	28411	28426	30477	30492	ACCTTTCAATAAACTG	23	H	1352
1485197	45057	45072	47123	47138	ATAACTATATCCAGGT	28	H	1353
1485204	23860	23875	25926	25941	ATTGAATACATTGTCT	27	H	1354
1485265	41790	41805	43856	43871	AATATCTCCTCTAGCC	42	H	1355
1485282	38904	38919	40970	40985	GTATTAGAGAATTCAC	30	H	1356
1485295	37909	37924	39975	39990	ATACATCACATTGTCC	31	H	1357
1485329	33075	33090	35141	35156	GATCCTTAAATTGTGC	28	H	1358
1485335	32730	32745	34796	34811	TGGGATAGCTATTACT	30	H	1359
1485356	39818	39833	41884	41899	GAATAATGTACCATCA	28	H	1360
1485363	43690	43705	45756	45771	CTAGAAGTATCATCAA	35	H	1361
1485383	15676	15691	17742	17757	CAAGTTTAAACGATCAG	23	H	1362
1485400	44767	44782	46833	46848	TATAGCACCTGACACT	58	H	1363
1485431	20815	20830	22881	22896	TTACATACCACATTGC	13	H	1364
1485507	32112	32127	34178	34193	ATATCAATTAACAGGT	28	H	1365
1485517	25812	25827	27878	27893	TTTGATAGACTTCCAA	29	H	1366
1485531	21225	21240	23291	23306	CCATATTGTTCTCAGA	11	H	1367
1485614	86388	86403	88454	88469	GGTAATTTTGTACTGT	34	H	1368
1485615	21805	21820	23871	23886	CATCCTACATTTAACA	43	H	1369
1485619	40546	40561	42612	42627	CAGTTAGAGCTATTAA	20	H	1370
1485651	17816	17831	19882	19897	GAAATCTTACGAAGCT	15	H	1371
1485660	23004	23019	25070	25085	TTATTCATCACAATCC	13	H	1372
1485662	43264	43279	45330	45345	TGTCATATCACTTCCT	40	H	1373
1485798	27964	27979	30030	30045	CGTGATAGTATTAAGT	21	H	1374
1485838	40185	40200	42251	42266	AGAATAATGAACCTTA	30	H	1375
1485883	15098	15113	17164	17179	ACAGCATAAGAAACGG	35	H	1376
1485925	26616	26631	28682	28697	GACTTTTGAATCAGTC	88	H	1377
1485941	33567	33582	35633	35648	GTATTTGAAATTATGC	52	H	1378
1486026	96037	96052	98103	98118	GACACCTACATGCTCA	37	H	1379
1486124	37383	37398	39449	39464	GCACAATTGGCCCTGG	26	H	1380
1486126	31465	31480	33531	33546	AGAGCAAAATTTTCGCA	18	H	1381
1486133	87180	87195	89246	89261	ATTTATAGACTTCCCA	49	H	1382
1486191	39444	39459	41510	41525	TAAATTTTCTAGCCAC	25	H	1383
1486206	30999	31014	33065	33080	GATTCTTCATTTACTA	16	H	1384
1486305	18732	18747	20798	20813	ATTTTTTAGCATCCCA	21	H	1385
1486338	34981	34996	37047	37062	CAAACCTGGCTTACGTA	47	H	1386
1486343	21442	21457	23508	23523	GACTATTAACCACTGA	38	H	1387
1486382	23473	23488	25539	25554	GATGAATTGCCACTAT	25	H	1388
1486406	36920	36935	38986	39001	GTTATAATTGATATGA	32	H	1389
1486415	19338	19353	21404	21419	CTAATGTACTAAACAC	29	H	1390
1486427	20338	20353	22404	22419	AACATACATCATCTGA	42	H	1391
1486489	29148	29163	31214	31229	ATACTTGTCTACCTAG	55	H	1392

1486492	44175	44190	46241	46256	GATTTATGTAACAGGA	23	H	1393
1486515	50945	50960	53011	53026	CGCATACTAATTCTTC	14	H	1394
1486605	38589	38604	40655	40670	CTATCCAAACCTTCAT	55	H	1395
1486627	26141	26156	28207	28222	TGTACATAAGCCACAT	34	H	1396
1486650	48890	48905	50956	50971	AAGTACTTTGATGAAT	39	H	1397
1486704	17128	17143	19194	19209	GTGAATAACACTTTGG	15	H	1398
1482206	2624	2639	4690	4705	ATTCCTTTACACCACA	45	I	1399
1482290	36473	36488	38539	38554	AGTCAATCAATTCTTG	12	I	1400
1483241	18733	18748	20799	20814	GATTTTTTAGCATCCC	5	I	1401
1483255	48845	48860	50911	50926	TCTGCAATAATATTAT	54	I	1402
1483385	29152	29167	31218	31233	GAAGATACTTGTCTAC	30	I	1403
1483433	2655	2670	4721	4736	GTCCTTTCATGAATAC	19	I	1404
1483539	71194	71209	73260	73275	CATATCTCATAATCCA	55	I	1405
1483554	46503	46518	48569	48584	GCAAATTTCCACCATG	44	I	1406
1483586	19871	19886	21937	21952	TGGGATATGATAACGA	35	I	1407
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	8	I	19
1484500	48115	48130	50181	50196	GGAAAACCATCTCTGC	48	I	1408
1484509	34982	34997	37048	37063	TCAAACCTGGCTTACGT	35	I	1409
1484595	15109	15124	17175	17190	ATGTACGAATAACAGC	67	I	1410
1484609	33082	33097	35148	35163	GCATAGAGATCCTTAA	26	I	1411
1484637	31545	31560	33611	33626	TCAATTAAAATCTTGG	75	I	1412
1484718	30009	30024	32075	32090	TCATATAGAATTCTGA	35	I	1413
1484742	47421	47436	49487	49502	GCTGATTGAAATTTTC	17	I	1414
1484762	17129	17144	19195	19210	GGTGAATAACACTTTG	12	I	1415
1484779	22466	22481	24532	24547	AATATCACGTAAACAT	36	I	1416
1484837	43269	43284	45335	45350	CTATTTGTCATATCAC	51	I	1417
1484843	87677	87692	89743	89758	TATACAGCATCTATCC	71	I	1418
1484847	81271	81286	83337	83352	GTACCTATATATTCAA	54	I	1419
1484857	25294	25309	27360	27375	ATGTATGCTCACTTCC	38	I	1420
1484865	26142	26157	28208	28223	ATGTACATAAGCCACA	51	I	1421
1484902	23505	23520	25571	25586	TAGTATACCTTTGTAG	44	I	1422
1484966	24432	24447	26498	26513	ACCTAGAAGTATTCTC	52	I	1423
1484986	44771	44786	46837	46852	TCTTTATAGCACCTGA	25	I	1424
1485005	37402	37417	39468	39483	CCACTAATGTTCCCTG	15	I	1425
1485033	66233	66248	68299	68314	TTCAATACATGCACTC	33	I	1426
1485053	46220	46235	48286	48301	TGAAACAATCTCCTTG	30	I	1427
1485076	39819	39834	41885	41900	TGAATAATGTACCATC	54	I	1428
1485114	27357	27372	29423	29438	CTGGATACCAATACTG	37	I	1429
1485126	15694	15709	17760	17775	CAGTATTAATAAAGTGC	35	I	1430
1485156	25828	25843	27894	27909	GCATAATTTCAATGCT	58	I	1431
1485167	20820	20835	22886	22901	AACTTTTACATACCAC	21	I	1432
1485192	96098	96113	98164	98179	GAGTATCATGATTTTC	37	I	1433
1485221	38911	38926	40977	40992	TCAACCAGTATTAGAG	30	I	1434

1485229	40186	40201	42252	42267	AAGAATAATGAACCTT	68	I	1435
1485288	86389	86404	88455	88470	AGGTAATTTTGTACTG	31	I	1436
1485321	16381	16396	18447	18462	GAAATTCCAAGACTTA	19	I	1437
1485451	27975	27990	30041	30056	GTAATAACCAACGTGA	23	I	1438
1485652	40552	40567	42618	42633	TGTTACCAGTTAGAGC	41	I	1439
1485717	85964	85979	88030	88045	ATGTAGCAACCTTTTT	64	I	1440
1485726	30305	30320	32371	32386	GTCCAATTGCCATTCT	22	I	1441
1485730	18267	18282	20333	20348	ATGCCTTAAATGCAGG	25	I	1442
1485755	33912	33927	35978	35993	AGTACTAATGACTATC	15	I	1443
1485767	21443	21458	23509	23524	AGACTATTAACCACTG	34	I	1444
1485771	28424	28439	30490	30505	CTCAATCCTTGTACC	64	I	1445
1485772	45489	45504	47555	47570	TGAATTACTTTACGTT	19	I	1446
1485774	41331	41346	43397	43412	AAACCCATGTAACGAC	38	I	1447
1485783	19339	19354	21405	21420	TCTAATGTACTAAACA	46	I	1448
1485863	32743	32758	34809	34824	TCTAAATAGATCTGG	22	I	1449
1485873	48891	48906	50957	50972	CAAGTACTTTGATGAA	14	I	1450
1485874	26643	26658	28709	28724	ACTTTTAAGAGTCTAT	44	I	1451
1485946	17817	17832	19883	19898	TGAAATCTTACGAAGC	24	I	1452
1485955	37910	37925	39976	39991	AATACATCACATTGTC	36	I	1453
1485966	35914	35929	37980	37995	TACTGTATCTAGACTG	61	I	1454
1486008	38591	38606	40657	40672	TCCTATCCAAACCTTC	58	I	1455
1486020	44176	44191	46242	46257	GGATTTATGTAACAGG	29	I	1456
1486120	41795	41810	43861	43876	AGTTAAATATCTCCTC	68	I	1457
1486125	21227	21242	23293	23308	AACCATATTGTTCTCA	9	I	1458
1486148	50991	51006	53057	53072	CATTTTACTTAAGTGG	37	I	1459
1486160	45058	45073	47124	47139	CATAACTATATCCAGG	24	I	1460
1486186	87181	87196	89247	89262	TATTTATAGACTTCCC	34	I	1461
1486195	21827	21842	23893	23908	ACAATACAATAAGTT	89	I	1462
1486239	23861	23876	25927	25942	AATTGAATACATTGTC	29	I	1463
1486321	39490	39505	41556	41571	GCAATACCATCCATTA	19	I	1464
1486371	31002	31017	33068	33083	CTAGATTCTTCATTTA	37	I	1465
1486411	70815	70830	72881	72896	TACTAACTATAGTTGT	94	I	1466
1486441	74045	74060	76111	76126	CCAATCATAAATTCCC	16	I	1467
1486478	71939	71954	74005	74020	CCATACAATTTCTGTC	33	I	1468
1486514	32113	32128	34179	34194	TATATCAATTAACAGG	43	I	1469
1486520	43691	43706	45757	45772	ACTAGAAGTATCATCA	26	I	1470
1486522	104258	104273	106324	106339	ACTGATTATCATTTTCG	25	I	1471
1486581	36923	36938	38989	39004	GGAGTTATAATTGATA	21	I	1472
1486590	33582	33597	35648	35663	AAAGCAATTTACTGTG	15	I	1473
1486611	20339	20354	22405	22420	CAACATACATCATCTG	34	I	1474
1486670	23005	23020	25071	25086	ATTATTTCATCACAATC	40	I	1475
1482396	18734	18749	20800	20815	AGATTTTTTAGCATCC	12	J	1476
1482425	44772	44787	46838	46853	TTCTTTATAGCACCTG	14	J	1477

1482703	30381	30396	32447	32462	GATATTCCTAATCTTC	32	J	1478
1482942	2656	2671	4722	4737	AGTCCTTTCATGAATA	34	J	1479
1482949	33706	33721	35772	35787	TCTATTTGACTTCTGT	13	J	1480
1483147	2625	2640	4691	4706	AATTCCTTTACACCAC	30	J	1481
1483660	48846	48861	50912	50927	ATCTGCAATAATATTA	23	J	1482
1483804	19902	19917	21968	21983	TTAATCATCATGTAGA	17	J	1483
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	12	J	19
1483894	23507	23522	25573	25588	GTTAGTATACCTTTGT	18	J	1484
1483937	38615	38630	40681	40696	GCACTAATCTAGGCAT	18	J	1485
1484193	41815	41830	43881	43896	TTAATTCCACATGTTC	29	J	1486
1484242	29178	29193	31244	31259	GTTATTAGATAAATTGG	10	J	1487
1484329	36479	36494	38545	38560	TCATTGAGTCAATCAA	37	J	1488
1484484	21891	21906	23957	23972	TAAAGATAAGTATCTC	22	J	1489
1484518	27390	27405	29456	29471	GTTAATAGTTCTCTGT	12	J	1490
1484621	26733	26748	28799	28814	TTATACACAGCATGCA	18	J	1491
1484662	41332	41347	43398	43413	TAAACCCATGTAACGA	18	J	1492
1484712	31581	31596	33647	33662	GCAAAATCCATGTCTG	20	J	1493
1484720	23866	23881	25932	25947	CGCATAATTGAATACA	27	J	1494
1484739	36925	36940	38991	39006	CAGGAGTTATAATTGA	16	J	1495
1484753	71195	71210	73261	73276	TCATATCTCATAATCC	35	J	1496
1484784	38942	38957	41008	41023	GAGAAGCCTGCTATGC	38	J	1497
1484812	23009	23024	25075	25090	GTACATTATTCATCAC	13	J	1498
1484858	30010	30025	32076	32091	ATCATATAGAATTCTG	20	J	1499
1484888	25296	25311	27362	27377	GAATGTATGCTCACTT	51	J	1500
1484908	17200	17215	19266	19281	CTACATTCTAGAAGGG	17	J	1501
1484925	33084	33099	35150	35165	TTGCATAGAGATCCTT	13	J	1502
1484936	70821	70836	72887	72902	CACTATTACTAACTAT	54	J	1503
1485003	33913	33928	35979	35994	AAGTACTAATGACTAT	39	J	1504
1485024	27976	27991	30042	30057	CGTAATAACCAACGTG	20	J	1505
1485092	71940	71955	74006	74021	TCCATACAATTTCTGT	23	J	1506
1485095	40584	40599	42650	42665	AATACAGCACAATTGT	60	J	1507
1485109	51214	51229	53280	53295	GTTGTAAAAACAGTCT	15	J	1508
1485174	17848	17863	19914	19929	ACTAATTTAATCTGAG	27	J	1509
1485189	44178	44193	46244	46259	TAGGATTTATGTAACA	20	J	1510
1485225	81272	81287	83338	83353	AGTACCTATATATTCA	32	J	1511
1485258	86442	86457	88508	88523	GACTTTATTGCTCAAA	26	J	1512
1485261	34983	34998	37049	37064	TTCAAACCTGGCTTACG	51	J	1513
1485277	43274	43289	45340	45355	GAACCTATTTGTCAT	23	J	1514
1485298	18281	18296	20347	20362	GCAATTTATATTGTAT	33	J	1515
1485313	47431	47446	49497	49512	TCAAACCTCATGCTGAT	34	J	1516
1485316	74046	74061	76112	76127	TCCAATCATAAATTCC	18	J	1517
1485386	40187	40202	42253	42268	GAAGAATAATGAACCT	24	J	1518
1485395	39491	39506	41557	41572	AGCAATACCATCCATT	16	J	1519

1485399	19343	19358	21409	21424	TTATTCTAATGTACTA	39	J	1520
1485462	20340	20355	22406	22421	GCAACATACATCATCT	32	J	1521
1485481	39820	39835	41886	41901	TTGAATAATGTACCAT	19	J	1522
1485496	87185	87200	89251	89266	CTCATATTTATAGACT	20	J	1523
1485554	24433	24448	26499	26514	CACCTAGAACTATTCT	27	J	1524
1485621	15121	15136	17187	17202	GTATTATCACATATGT	41	J	1525
1485638	20821	20836	22887	22902	CAACTTTTACATACCA	8	J	1526
1485683	16382	16397	18448	18463	AGAAATTTCCAAGACTT	31	J	1527
1485697	31007	31022	33073	33088	TTTGACTAGATTCTTC	33	J	1528
1485723	45059	45074	47125	47140	TCATAACTATATCCAG	11	J	1529
1485839	46263	46278	48329	48344	CAACGTCTAGTATGAG	18	J	1530
1485907	48162	48177	50228	50243	GGACAATTCCAGCAGC	27	J	1531
1485929	15721	15736	17787	17802	GGCTAAGATATTTTGG	57	J	1532
1485934	46504	46519	48570	48585	AGCAAATTTCCACCAT	52	J	1533
1485999	96487	96502	98553	98568	GCCTTACTTCGTTTGC	36	J	1534
1486006	87679	87694	89745	89760	CTTATACAGCATCTAT	46	J	1535
1486027	21445	21460	23511	23526	ACAGACTATTAACCAC	14	J	1536
1486081	22470	22485	24536	24551	CTTGAATATCACGTAA	22	J	1537
1486093	32744	32759	34810	34825	GTCTAAAATAGATCTG	12	J	1538
1486190	35940	35955	38006	38021	GTGAAATAAAGTTCCT	11	J	1539
1486234	45490	45505	47556	47571	ATGAATTACTTTACGT	25	J	1540
1486251	66282	66297	68348	68363	GTCAATATAGTCTCTG	11	J	1541
1486278	26143	26158	28209	28224	TATGTACATAAGCCAC	11	J	1542
1486310	43701	43716	45767	45782	CAGTATTATTACTAGA	20	J	1543
1486329	28432	28447	30498	30513	AACTATGACTCAATCC	21	J	1544
1486330	48920	48935	50986	51001	CCAATTAATGTACTAT	37	J	1545
1486353	37911	37926	39977	39992	GAATACATCACATTGT	36	J	1546
1486391	104442	104457	106508	106523	GCATTTGACACACAGA	25	J	1547
1486521	85965	85980	88031	88046	TATGTAGCAACCTTTT	67	J	1548
1486668	21228	21243	23294	23309	AAACCATATTGTTCTC	19	J	1549
1486675	32178	32193	34244	34259	GCATTTCTAGCTTAGG	10	J	1550
1486691	25829	25844	27895	27910	TGCATAATTTCAATGC	81	J	1551
1486699	37449	37464	39515	39530	CATAGTAGCACTCCAC	37	J	1552
1482551	2627	2642	4693	4708	TGAATTCCTTTACACC	23	K	1553
1483162	48847	48862	50913	50928	TATCTGCAATAATATT	45	K	1554
1483375	2657	2672	4723	4738	AAGTCCTTTCATGAAT	32	K	1555
1483627	37515	37530	39581	39596	CTGGATACTTTGTTGT	33	K	1556
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	17	K	19
1484274	21929	21944	23995	24010	ACTTTTATATACGTGT	19	K	1557
1484529	20823	20838	22889	22904	ACCAACTTTTACATAC	33	K	1558
1484589	21448	21463	23514	23529	CTTACAGACTATTAAC	39	K	1559
1484655	81545	81560	83611	83626	ATGTTTATTTTACGCGA	19	K	1560
1484743	25858	25873	27924	27939	AATTCTTAGACATGCG	14	K	1561

1484794	41339	41354	43405	43420	GCATTAATAAACCCAT	19	K	1562
1484796	44851	44866	46917	46932	TAAATACCTACTAGCA	59	K	1563
1484818	16397	16412	18463	18478	GTTACTCCAAGGAAGA	12	K	1564
1484874	43702	43717	45768	45783	ACAGTATTATTACTAG	14	K	1565
1484882	45061	45076	47127	47142	GTTCATAACTATATCC	11	K	1566
1484899	32745	32760	34811	34826	AGTCTAAAATAGATCT	23	K	1567
1484931	51250	51265	53316	53331	GCATTTGCATTACTAA	28	K	1568
1484939	41817	41832	43883	43898	ACTTAATTCCACATGT	40	K	1569
1484944	30405	30420	32471	32486	GAGCGATCGGAAGCTC	88	K	1570
1484961	40216	40231	42282	42297	AGTAAACATGCCAGGT	47	K	1571
1484963	104837	104852	106903	106918	GAGTATTCATGACTTG	44	K	1572
1485011	38970	38985	41036	41051	ACTATATGACAAACAT	35	K	1573
1485028	87186	87201	89252	89267	GCTCATATTTATAGAC	26	K	1574
1485058	26144	26159	28210	28225	ATATGTACATAAGCCA	24	K	1575
1485065	34987	35002	37053	37068	ACCTTTCAAACCTGGCT	27	K	1576
1485083	33106	33121	35172	35187	AATGCTAAAATATGGG	16	K	1577
1485100	24474	24489	26540	26555	TCCAATTAACCTGTGG	28	K	1578
1485110	20342	20357	22408	22423	TGGCAACATACATCAT	49	K	1579
1485187	33757	33772	35823	35838	GTGAATTACAATTTGT	91	K	1580
1485216	25313	25328	27379	27394	TGACATATCAAGTTGG	21	K	1581
1485242	48472	48487	50538	50553	TAGTTATTCTCAGCGG	14	K	1582
1485247	17850	17865	19916	19931	GTACTAATTTAATCTG	27	K	1583
1485275	46505	46520	48571	48586	TAGCAAATTTCCACCA	50	K	1584
1485315	18304	18319	20370	20385	TTAAGCACTTTCATGC	32	K	1585
1485344	45491	45506	47557	47572	CATGAATTACTTTACG	32	K	1586
1485369	23950	23965	26016	26031	TCCAACCCTGGGCAGT	36	K	1587
1485405	44190	44205	46256	46271	CACGACACAGTTTAGG	18	K	1588
1485467	27392	27407	29458	29473	TTGTTAATAGTTCTCT	17	K	1589
1485478	47432	47447	49498	49513	TTCAAACCTCATGCTGA	61	K	1590
1485514	86515	86530	88581	88596	GAATATTCCTTCGTGA	58	K	1591
1485600	26734	26749	28800	28815	TTTATACACAGCATGC	31	K	1592
1485635	23047	23062	25113	25128	GATAGTTAAAATCTAT	94	K	1593
1485643	21230	21245	23296	23311	ACAAACCATATTGTTC	31	K	1594
1485703	38649	38664	40715	40730	GCTAAACTACCGCTGC	89	K	1595
1485812	29201	29216	31267	31282	AAAGCCTTCTTAGTGG	27	K	1596
1485822	46270	46285	48336	48351	AATAGCCCAACGTCTA	54	K	1597
1485902	71941	71956	74007	74022	ATCCATACAATTTCTG	27	K	1598
1485910	37928	37943	39994	40009	GTCTAAAATCCTTTG	46	K	1599
1485914	15734	15749	17800	17815	AACATTGAATCTTGGC	61	K	1600
1485943	19903	19918	21969	21984	ATTAATCATCATGTAG	21	K	1601
1486011	31601	31616	33667	33682	AAGAATTAACCTTGGT	28	K	1602
1486036	39493	39508	41559	41574	AAAGCAATACCATCCA	24	K	1603
1486065	22473	22488	24539	24554	ACCCTTGAATATCACG	13	K	1604

1486119	27977	27992	30043	30058	TCGTAATAACCAACGT	44	K	1605
1486121	36958	36973	39024	39039	ACTACCAAATTTGTGT	88	K	1606
1486197	40585	40600	42651	42666	GAATACAGCACAATTG	85	K	1607
1486201	17220	17235	19286	19301	ATATTTCACTCTCATG	36	K	1608
1486245	33943	33958	36009	36024	GGGTATTAATATTTCA	11	K	1609
1486255	35941	35956	38007	38022	GGTGAAATAAAGTTCC	27	K	1610
1486258	74309	74324	76375	76390	ACCATTAAGACATTCA	20	K	1611
1486265	70856	70871	72922	72937	AATCTACTCAATTAGC	43	K	1612
1486283	19390	19405	21456	21471	ATAACTTCTTATGTGC	19	K	1613
1486287	48921	48936	50987	51002	CCCAATTAATGTACTA	39	K	1614
1486300	67146	67161	69212	69227	TTAAGATGATTCTTCA	52	K	1615
1486302	18736	18751	20802	20817	CCAGATTTTTTAGCAT	8	K	1616
1486311	36504	36519	38570	38585	CTTATTAATTTAGTCT	30	K	1617
1486326	28434	28449	30500	30515	ACAACATGACTCAAT	56	K	1618
1486401	15146	15161	17212	17227	CTTATTATCTACGTGT	47	K	1619
1486440	85973	85988	88039	88054	CAAGACATTATGTAGC	32	K	1620
1486501	87680	87695	89746	89761	TCTTATACAGCATCTA	53	K	1621
1486563	71266	71281	73332	73347	GGCATATAACAGTTGT	19	K	1622
1486568	32395	32410	34461	34476	CACCTTCAAACCCCTT	38	K	1623
1486573	43350	43365	45416	45431	GTCATTTAAATTCGAA	24	K	1624
1486576	31011	31026	33077	33092	TAGATTTGACTAGATT	13	K	1625
1486585	39821	39836	41887	41902	CTTGAATAATGTACCA	17	K	1626
1486603	23508	23523	25574	25589	TGTTAGTATACCTTTG	20	K	1627
1486608	30029	30044	32095	32110	ATTACTAACGTGCAGT	25	K	1628
1486708	96902	96917	98968	98983	AAGATTATATTGTTGT	32	K	1629
1482229	48934	48949	51000	51015	CTCATAAAAACCTCCC	42	L	1630
1482809	48848	48863	50914	50929	ATATCTGCAATAATAT	64	L	1631
1483048	40592	40607	42658	42673	GCTGTATGAATACAGC	123	L	1632
1483640	74431	74446	76497	76512	CTTATTCAACTCCTCA	57	L	1633
1483733	2658	2673	4724	4739	AAAGTCCTTTTCATGAA	28	L	1634
1483790	2628	2643	4694	4709	ATGAATTCCTTTACAC	24	L	1635
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	7	L	19
1484495	87193	87208	89259	89274	GCTTTAAGCTCATATT	42	L	1636
1484559	28435	28450	30501	30516	TACAACATGACTCAA	55	L	1637
1484575	39508	39523	41574	41589	AGACAAACTTGATCTA	68	L	1638
1484606	37929	37944	39995	40010	AGTCCTAAAATCCTTT	31	L	1639
1484656	37561	37576	39627	39642	GACTACACCACGGTTT	61	L	1640
1484676	43351	43366	45417	45432	AGTCATTTAAATTCGA	11	L	1641
1484703	24558	24573	26624	26639	CTGATAATCTCTCTAA	23	L	1642
1484708	23510	23525	25576	25591	AATGTTAGTATACCTT	15	L	1643
1484731	31046	31061	33112	33127	CCAGATCAAACATTAA	19	L	1644
1484765	23073	23088	25139	25154	ACTTATGTCACCCCAT	43	L	1645
1484790	46272	46287	48338	48353	ACAATAGCCCAACGTC	53	L	1646

1484795	104905	104920	106971	106986	CCAATTTACAACCTGTG	46	L	1647
1484819	33969	33984	36035	36050	AAACCTTTCATTGTCC	46	L	1648
1484836	31602	31617	33668	33683	GAAGAATTAACCTTGG	31	L	1649
1484854	22474	22489	24540	24555	TACCTTGAATATCAC	30	L	1650
1484867	38650	38665	40716	40731	AGCTAAACTACCGCTG	95	L	1651
1484877	41819	41834	43885	43900	CAACTTAATTCCACAT	32	L	1652
1484879	19904	19919	21970	21985	TATTAATCATCATGTA	43	L	1653
1484922	15737	15752	17803	17818	CCAAACATTGAATCTT	58	L	1654
1484932	38975	38990	41041	41056	CATGAACATATGACA	26	L	1655
1484991	17866	17881	19932	19947	CTGATTAATTGCCTGT	26	L	1656
1485012	26161	26176	28227	28242	ATTTATTCCACGTCTT	28	L	1657
1485048	18307	18322	20373	20388	AGATTAAGCACTTTCA	16	L	1658
1485101	21231	21246	23297	23312	AACAAACCATATTGTT	57	L	1659
1485103	30032	30047	32098	32113	AAAATTACTAACGTGC	31	L	1660
1485133	44852	44867	46918	46933	ATAAATACCTACTAGC	38	L	1661
1485135	16470	16485	18536	18551	GATGATGTCACTATAA	11	L	1662
1485163	32746	32761	34812	34827	GAGTCTAAAATAGATC	19	L	1663
1485198	21930	21945	23996	24011	CACTTTTATATACGTG	38	L	1664
1485266	20833	20848	22899	22914	AGTGAGAAATACCAAC	62	L	1665
1485267	27978	27993	30044	30059	ATCGTAATAACCAACG	65	L	1666
1485270	24008	24023	26074	26089	TATAATGCACTACAAT	49	L	1667
1485350	67243	67258	69309	69324	CTTATATCTACATCAT	29	L	1668
1485491	51317	51332	53383	53398	CCAGATCAATCCCAGT	35	L	1669
1485538	18750	18765	20816	20831	TTCATTGAAACCATCC	37	L	1670
1485610	70861	70876	72927	72942	GCTATAATCTACTCAA	52	L	1671
1485642	20445	20460	22511	22526	TTAAGATTATGCCTGT	35	L	1672
1485661	32402	32417	34468	34483	TAGGGATCACCTTCAA	40	L	1673
1485665	48473	48488	50539	50554	CTAGTTATTCTCAGCG	18	L	1674
1485694	33758	33773	35824	35839	AGTGAATTACAATTTG	20	L	1675
1485722	85979	85994	88045	88060	AGCTATCAAGACATTA	53	L	1676
1485727	44195	44210	46261	46276	ACTAACACGACACAGT	78	L	1677
1485743	47606	47621	49672	49687	ATAAATTCTGCATAGC	35	L	1678
1485764	86517	86532	88583	88598	TGGAATATTCTTCGT	29	L	1679
1485790	26738	26753	28804	28819	GTATTTTATACACAGC	9	L	1680
1485795	81674	81689	83740	83755	GCACATTTACACCAGT	24	L	1681
1485816	71978	71993	74044	74059	AATACTGACACTTGTG	39	L	1682
1485827	30468	30483	32534	32549	AGGCATTACTTTTCAA	23	L	1683
1485948	97449	97464	99515	99530	CTGTATTTAATGCTGC	12	L	1684
1485968	25334	25349	27400	27415	CATTCATACAGACGTG	49	L	1685
1485995	41340	41355	43406	43421	TGCATTAATAAACCCA	26	L	1686
1486007	17265	17280	19331	19346	GAAACTCTCCCAGACA	22	L	1687
1486061	27414	27429	29480	29495	CCAATTACTCCTACAA	16	L	1688
1486097	71267	71282	73333	73348	TGGCATATAACAGTTG	20	L	1689

1486101	46506	46521	48572	48587	ATAGCAAATTTCCACC	63	L	1690
1486103	45496	45511	47562	47577	TATAGCATGAATTACT	35	L	1691
1486104	39822	39837	41888	41903	ACTTGAATAATGTACC	21	L	1692
1486122	33127	33142	35193	35208	ATTACCCCATAGCTTA	30	L	1693
1486204	19391	19406	21457	21472	GATAACTTCTTATGTG	36	L	1694
1486218	43743	43758	45809	45824	TTCAATTACCACTGCA	21	L	1695
1486253	25899	25914	27965	27980	TGTGATAAACATCTTC	6	L	1696
1486292	87681	87696	89747	89762	TTCTTATACAGCATCT	49	L	1697
1486349	29207	29222	31273	31288	GACATAAAAGCCTTCT	55	L	1698
1486384	21449	21464	23515	23530	GCTTACAGACTATTAA	44	L	1699
1486416	36959	36974	39025	39040	AACTACCAAATTTGTG	61	L	1700
1486448	45120	45135	47186	47201	TATTTTGCCTAACCTC	76	L	1701
1486479	15149	15164	17215	17230	CTACTTATTATCTACG	58	L	1702
1486493	40218	40233	42284	42299	CAAGTAAACATGCCAG	27	L	1703
1486500	36505	36520	38571	38586	ACTTATTAATTTAGTC	59	L	1704
1486523	34988	35003	37054	37069	AACCTTTCAAACTGGC	15	L	1705
1486587	35962	35977	38028	38043	ACAACCATAATTTGTA	67	L	1706
1482260	36522	36537	38588	38603	AGTACAAATAGATGTG	38	M	1707
1482670	44856	44871	46922	46937	GTCTATAAATACCTAC	26	M	1708
1483112	48850	48865	50916	50931	CAATATCTGCAATAAT	43	M	1709
1483228	40711	40726	42777	42792	TGGAATTATAGTATGT	23	M	1710
1483333	30485	30500	32551	32566	GAGAACTTTGTTTTGG	12	M	1711
1483391	40306	40321	42372	42387	CCCATTTAAACTTTCC	27	M	1712
1483489	2659	2674	4725	4740	GAAAGTCCTTTCATGA	21	M	1713
1483785	18308	18323	20374	20389	AAGATTAAGCACTTTC	16	M	1714
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	11	M	19
1483967	20473	20488	22539	22554	CTTATTACTACCTTGT	23	M	1715
1484063	2630	2645	4696	4711	TAATGAATTCCTTTAC	48	M	1716
1484506	41383	41398	43449	43464	AATCATATGCACTCAT	46	M	1717
1484541	18833	18848	20899	20914	TTCTATTTACCAGGGT	6	M	1718
1484598	37980	37995	40046	40061	ACTATAGCCTTTCATA	67	M	1719
1484601	20860	20875	22926	22941	TATGTACCATTAGTGG	39	M	1720
1484622	27100	27115	29166	29181	AGCACAACAAATAGGT	20	M	1721
1484704	33134	33149	35200	35215	ACAATATATTACCCCA	23	M	1722
1484706	24009	24024	26075	26090	GTATAATGCACTACAA	41	M	1723
1484804	43744	43759	45810	45825	CTTCAATTACCACTGC	33	M	1724
1484806	17268	17283	19334	19349	TTGGAAACTCTCCAG	46	M	1725
1484813	39833	39848	41899	41914	CATAATAATCGACTTG	31	M	1726
1484842	32423	32438	34489	34504	GAATCATTACTGGTTG	10	M	1727
1484849	16483	16498	18549	18564	CCATTTAATAAGAGAT	24	M	1728
1484852	31056	31071	33122	33137	ATGGTTTCAACCAGAT	62	M	1729
1484855	21450	21465	23516	23531	TGCTTACAGACTATTA	17	M	1730
1484860	21236	21251	23302	23317	CTTGTAACAAACCATA	33	M	1731

1484903	30034	30049	32100	32115	ACAAAATTACTAACGT	37	M	1732
1484938	47699	47714	49765	49780	TAGATAAGTCTCTCAT	32	M	1733
1484976	72004	72019	74070	74085	TGCTATCAAGATATGG	31	M	1734
1484995	45122	45137	47188	47203	TATATTTTGCCTAACC	92	M	1735
1485000	48935	48950	51001	51016	TCTCATAAAAACCTCC	28	M	1736
1485071	26162	26177	28228	28243	CATTTATTCCACGTCT	26	M	1737
1485087	23074	23089	25140	25155	GACTTATGTCACCCCA	44	M	1738
1485113	27979	27994	30045	30060	AATCGTAATAACCAAC	21	M	1739
1485117	87233	87248	89299	89314	ACATTCTACACAATCT	38	M	1740
1485125	21937	21952	24003	24018	TAGGAATCACTTTTAT	40	M	1741
1485219	31658	31673	33724	33739	ACGAATGCAAATTTTC	20	M	1742
1485227	22503	22518	24569	24584	CAATTGGCATCTCATT	67	M	1743
1485299	19393	19408	21459	21474	CTGATAACTTCTTATG	30	M	1744
1485300	15766	15781	17832	17847	ACCAAGATGTCCAAGT	87	M	1745
1485387	37564	37579	39630	39645	ACTGACTACACCACGG	31	M	1746
1485409	71302	71317	73368	73383	GATATGACCTGTTATT	53	M	1747
1485440	86518	86533	88584	88599	TTGGAATATTCCCTCG	33	M	1748
1485444	43402	43417	45468	45483	CCATATTGCCATCTAA	38	M	1749
1485454	87757	87772	89823	89838	TTTATTAGAGCCCCCA	50	M	1750
1485477	15150	15165	17216	17231	CCTACTTATTATCTAC	61	M	1751
1485495	81702	81717	83768	83783	TTCAATTTCTAGTCAC	32	M	1752
1485515	27415	27430	29481	29496	ACCAATTACTCCTACA	43	M	1753
1485521	85980	85995	88046	88061	AAGCTATCAAGACATT	41	M	1754
1485608	46507	46522	48573	48588	AATAGCAAATTTCCAC	65	M	1755
1485663	70891	70906	72957	72972	TTACCCACTTTTTCCT	80	M	1756
1485704	48475	48490	50541	50556	TACTAGTTATTCTCAG	34	M	1757
1485729	38651	38666	40717	40732	AAGCTAAACTACCGCT	97	M	1758
1485733	67244	67259	69310	69325	TCTTATATCTACATCA	52	M	1759
1485776	29208	29223	31274	31289	AGACATAAAAGCCTTC	16	M	1760
1485787	32774	32789	34840	34855	GAGAACAAGACATTGA	30	M	1761
1485808	74432	74447	76498	76513	TCTTATTCAACTCCTC	74	M	1762
1485819	41820	41835	43886	43901	ACAACCTTAATTCCACA	31	M	1763
1485871	25911	25926	27977	27992	TATAATCAATTCTGTG	32	M	1764
1485876	23551	23566	25617	25632	CTAGCAGAACACTTGT	38	M	1765
1485898	46276	46291	48342	48357	CTTTACAATAGCCCAA	42	M	1766
1485944	28436	28451	30502	30517	ATACAACCTATGACTCA	45	M	1767
1485959	36008	36023	38074	38089	ATCTTACATTACATA	47	M	1768
1486014	52007	52022	54073	54088	GTATAATCGTGACTAA	39	M	1769
1486092	39069	39084	41135	41150	GAACAGATTCCAGCAG	49	M	1770
1486110	45502	45517	47568	47583	TGATATTATAGCATGA	13	M	1771
1486117	39512	39527	41578	41593	GGTTAGACAAACTTGA	25	M	1772
1486162	34989	35004	37055	37070	CAACCTTTCAAACCTGG	30	M	1773
1486170	97614	97629	99680	99695	ACATTACTGAACCTCTC	35	M	1774

1486320	17867	17882	19933	19948	ACTGATTAATTGCCTG	20	M	1775
1486322	33777	33792	35843	35858	AACCACTGAACCTTGA	50	M	1776
1486379	25339	25354	27405	27420	GCAAACATTCATACAG	36	M	1777
1486387	19906	19921	21972	21987	ACTATTAATCATCATG	36	M	1778
1486428	36961	36976	39027	39042	CCAACTACCAAATTTG	61	M	1779
1486509	33970	33985	36036	36051	CAAACCTTTTCATTGTC	43	M	1780
1486534	104906	104921	106972	106987	TCCAATTTACAACCTGT	43	M	1781
1486599	24559	24574	26625	26640	CCTGATAATCTCTCTA	20	M	1782
1486643	44196	44211	46262	46277	GACTAACACGACACAG	101	M	1783
1482194	18387	18402	20453	20468	ATCACTTAGATTCTG	14	N	1784
1482577	34996	35011	37062	37077	TAGAATGCAACCTTTC	51	N	1785
1482982	2631	2646	4697	4712	CTAATGAATTCCTTTA	60	N	1786
1483367	26163	26178	28229	28244	GCATTTATTCCACGTC	11	N	1787
1483383	46277	46292	48343	48358	TCTTTACAATAGCCCA	29	N	1788
1483673	32425	32440	34491	34506	TCGAATCATTACTGGT	15	N	1789
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	13	N	19
1484147	2660	2675	4726	4741	TGAAAGTCCTTTCATG	48	N	1790
1484175	15480	15495	17546	17561	ACAATACATACTTCTA	56	N	1791
1484247	48852	48867	50918	50933	ATCAATATCTGCAATA	33	N	1792
1484514	33971	33986	36037	36052	ACAAACCTTTTCATTGT	105	N	1793
1484516	20861	20876	22927	22942	TTATGTACCATTAGTG	40	N	1794
1484520	33778	33793	35844	35859	CAACCACTGAACCTTGG	32	N	1795
1484525	37715	37730	39781	39796	GATATATTCCTGAGAC	23	N	1796
1484611	15768	15783	17834	17849	CCACCAAGATGTCCAA	47	N	1797
1484636	27418	27433	29484	29499	ACAACCAATTACTCCT	41	N	1798
1484642	87239	87254	89305	89320	GTTTTAACATTCTACA	41	N	1799
1484647	40308	40323	42374	42389	GACCCATTTAAACTTT	89	N	1800
1484658	53043	53058	55109	55124	ATCATAAATCAGTCCT	28	N	1801
1484659	36978	36993	39044	39059	CCTTTATAAAGTCTCC	19	N	1802
1484680	23563	23578	25629	25644	TATAGACCATCTCTAG	39	N	1803
1484686	81790	81805	83856	83871	AGGTATATAGTACCAG	44	N	1804
1484726	18873	18888	20939	20954	AGTCATTAATAAGCAT	20	N	1805
1484734	40712	40727	42778	42793	CTGGAATTATAGTATG	17	N	1806
1484746	44197	44212	46263	46278	TGACTAACACGACACA	51	N	1807
1484751	36542	36557	38608	38623	ACCTTATAAGTAAGCA	21	N	1808
1484787	16484	16499	18550	18565	GCCATTTAATAAGAGA	49	N	1809
1484797	44857	44872	46923	46938	TGTCTATAAATACCTA	16	N	1810
1484799	29209	29224	31275	31290	GAGACATAAAAGCCTT	56	N	1811
1484830	20474	20489	22540	22555	TCTTATTACTACCTTG	67	N	1812
1484831	41821	41836	43887	43902	TACAACTTAATTCCAC	58	N	1813
1484851	22511	22526	24577	24592	GACAAATACAATTGGC	22	N	1814
1484878	17891	17906	19957	19972	CGTGAAAAGGGTCGGA	20	N	1815
1484960	36011	36026	38077	38092	TAAATCTTACATTCAC	28	N	1816

1485025	33135	33150	35201	35216	TACAATATATTACCCC	42	N	1817
1485042	43404	43419	45470	45485	CTCCATATTGCCATCT	38	N	1818
1485139	31674	31689	33740	33755	ACATAACAAACACTAG	46	N	1819
1485179	17287	17302	19353	19368	GTTAATTGTCTACTGT	13	N	1820
1485215	27122	27137	29188	29203	ACAGCTAGATGTCAAT	30	N	1821
1485243	47700	47715	49766	49781	ATAGATAAGTCTCTCA	34	N	1822
1485269	32794	32809	34860	34875	AATGATTCCAGTCTGA	49	N	1823
1485374	25945	25960	28011	28026	CAAACCTTCTAGCACTA	31	N	1824
1485376	71303	71318	73369	73384	AGATATGACCTGTTAT	68	N	1825
1485422	74514	74529	76580	76595	AAGATTTATCCTCCAA	38	N	1826
1485437	43768	43783	45834	45849	TTAATACATGTTCCCA	40	N	1827
1485446	41384	41399	43450	43465	CAATCATATGCACTCA	41	N	1828
1485452	19907	19922	21973	21988	AACTATTAATCATCAT	56	N	1829
1485489	72011	72026	74077	74092	AAGTTATTGCTATCAA	62	N	1830
1485572	46508	46523	48574	48589	GAATAGCAAATTTCCA	71	N	1831
1485586	27980	27995	30046	30061	AAATCGTAATAACCAA	26	N	1832
1485625	30056	30071	32122	32137	ATACCCTCATATTCTA	37	N	1833
1485711	87759	87774	89825	89840	TTTTTATTAGAGCCCC	79	N	1834
1485750	39835	39850	41901	41916	GACATAATAATCGACT	22	N	1835
1485852	31068	31083	33134	33149	TGTTAAGCTAAAATGG	25	N	1836
1485909	21452	21467	23518	23533	AATGCTTACAGACTAT	53	N	1837
1486032	45503	45518	47569	47584	ATGATATTATAGCATG	29	N	1838
1486116	45125	45140	47191	47206	GATTATATTTTGCCTA	58	N	1839
1486163	25558	25573	27624	27639	ATTACCTTTCATTAGC	43	N	1840
1486164	24597	24612	26663	26678	GACTATAAAAAGAATGG	31	N	1841
1486166	19395	19410	21461	21476	GACTGATAAATTCTTA	28	N	1842
1486167	39072	39087	41138	41153	AGTGAACAGATTCCAG	55	N	1843
1486181	39515	39530	41581	41596	ACGGGTTAGACAAACT	15	N	1844
1486185	21238	21253	23304	23319	TACTTGTAACAAACCA	30	N	1845
1486187	70893	70908	72959	72974	AGTTACCCACTTTTTC	40	N	1846
1486334	97823	97838	99889	99904	TCCATTAAGTCCATGG	87	N	1847
1486376	21982	21997	24048	24063	GCAAAGATAACCATAT	30	N	1848
1486408	49022	49037	51088	51103	ACTGATTAAGTGTATT	62	N	1849
1486496	48476	48491	50542	50557	GTACTAGTTATTCTCA	32	N	1850
1486532	85981	85996	88047	88062	GAAGCTATCAAGACAT	54	N	1851
1486536	37982	37997	40048	40063	AAACTATAGCCTTTCA	70	N	1852
1486558	24010	24025	26076	26091	TGTATAATGCACTACA	37	N	1853
1486579	38652	38667	40718	40733	AAAGCTAACTACCGC	55	N	1854
1486594	23184	23199	25250	25265	ACGTACACTGAAAGGG	22	N	1855
1486612	86561	86576	88627	88642	TAACATTTGTTCCAGG	25	N	1856
1486658	67249	67264	69315	69330	GATATTCTTATATCTA	69	N	1857
1486680	30519	30534	32585	32600	TGAGAAACTATTGAGT	54	N	1858
1486703	104998	105013	107064	107079	GACACAATTTTATCCC	31	N	1859

1486705	28437	28452	30503	30518	CATACAACTATGACTC	35	N	1860
1482333	44893	44908	46959	46974	ATATCAACATGCCATT	54	O	1861
1482405	16492	16507	18558	18573	GCAGATATGCCATTTA	28	O	1862
1482527	2632	2647	4698	4713	GCTAATGAATTCCTTT	24	O	1863
1483094	45127	45142	47193	47208	CTGATTATATTTTGCC	19	O	1864
1483235	48853	48868	50919	50934	CATCAATATCTGCAAT	44	O	1865
1483382	15481	15496	17547	17562	CACAATACATACTTCT	60	O	1866
1483468	2661	2676	4727	4742	TTGAAAGTCCTTTCAT	67	O	1867
1483728	29227	29242	31293	31308	TGGATAAAATTCAGAC	18	O	1868
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	11	O	19
1484479	98104	98119	100170	100185	CTGGTTTAGACCTTTC	45	O	1869
1484488	24011	24026	26077	26092	CTGTATAATGCACTAC	39	O	1870
1484505	46516	46531	48582	48597	TTGTAATAGAATAGCA	30	O	1871
1484523	87315	87330	89381	89396	AACTATACTTGAGCAC	29	O	1872
1484547	30057	30072	32123	32138	AATACCCTCATATTCT	50	O	1873
1484577	36979	36994	39045	39060	CCCTTTATAAAGTCTC	22	O	1874
1484630	34998	35013	37064	37079	TATAGAATGCAACCTT	61	O	1875
1484632	49024	49039	51090	51105	GAAGTGATTAAGTGT	56	O	1876
1484692	43769	43784	45835	45850	CTTAATACATGTTCCC	45	O	1877
1484750	67258	67273	69324	69339	CACATTGACGATATTC	38	O	1878
1484781	86097	86112	88163	88178	TTCAAGACTCCTTGTT	77	O	1879
1484946	17288	17303	19354	19369	TGTTAATTGTCTACTG	34	O	1880
1484974	27423	27438	29489	29504	ACCATACAACCAATTA	32	O	1881
1485026	19935	19950	22001	22016	GACATTTCAAGCTTAT	17	O	1882
1485041	86562	86577	88628	88643	TTAACATTTGTTCCAG	54	O	1883
1485044	72012	72027	74078	74093	CAAGTTATTGCTATCA	16	O	1884
1485194	31774	31789	33840	33855	GAATTCAGACAGAAGC	56	O	1885
1485226	30521	30536	32587	32602	CATGAGAACTATTGA	68	O	1886
1485260	21457	21472	23523	23538	ATTGTAATGCTTACAG	21	O	1887
1485273	37984	37999	40050	40065	GCAAACTATAGCCTTT	33	O	1888
1485280	21239	21254	23305	23320	ATACTTGTAAACAAACC	20	O	1889
1485307	23565	23580	25631	25646	GATATAGACCATCTCT	46	O	1890
1485325	41823	41838	43889	43904	AATACAACCTTAATTCC	32	O	1891
1485337	74555	74570	76621	76636	GCAACTAACCAACAGA	48	O	1892
1485341	33974	33989	36040	36055	GATACAAACCTTTCAT	44	O	1893
1485349	15803	15818	17869	17884	GCCATAGATAACTGAG	47	O	1894
1485362	32798	32813	34864	34879	TTGGAATGATTCCAGT	40	O	1895
1485473	71304	71319	73370	73385	TAGATATGACCTGTTA	52	O	1896
1485547	41388	41403	43454	43469	CTTACAATCATATGCA	20	O	1897
1485564	39582	39597	41648	41663	AGGAAGTTCACACATT	36	O	1898
1485585	26224	26239	28290	28305	CGAAGAATTACCCAGC	37	O	1899
1485590	19398	19413	21464	21479	TATGACTGATAACTTC	40	O	1900
1485616	81846	81861	83912	83927	GAGGTACAAAATCTGC	22	O	1901

1485628	27152	27167	29218	29233	TAGATAGACTCCTACA	58	O	1902
1485664	47701	47716	49767	49782	GATAGATAAGTCTCTC	27	O	1903
1485707	25585	25600	27651	27666	TCTAAATTCCAAGTGC	35	O	1904
1485713	105013	105028	107079	107094	TTCATATGACCATCAG	37	O	1905
1485715	32426	32441	34492	34507	CTCGAATCATTACTGG	34	O	1906
1485769	46278	46293	48344	48359	TTCTTTACAATAGCCC	34	O	1907
1485867	44273	44288	46339	46354	CCATTGATTTAATACA	74	O	1908
1485878	22512	22527	24578	24593	TGACAAATACAATTGG	15	O	1909
1485901	45504	45519	47570	47585	GATGATATTATAGCAT	28	O	1910
1485981	27981	27996	30047	30062	TAAATCGTAATAACCA	35	O	1911
1486015	70897	70912	72963	72978	ACGTAGTTACCCACTT	63	O	1912
1486029	53503	53518	55569	55584	ATCAATCGGTACTTAT	81	O	1913
1486075	87762	87777	89828	89843	ACTTTTTTATTAGAGC	63	O	1914
1486102	37716	37731	39782	39797	AGATATATTCCTGAGA	33	O	1915
1486135	39856	39871	41922	41937	CGTCGTAAACTGCAT	34	O	1916
1486189	24716	24731	26782	26797	TCTACTTAGACCTGCC	38	O	1917
1486193	33804	33819	35870	35885	GTAATAGCCTTTATGA	51	O	1918
1486238	31099	31114	33165	33180	ATCAATTGATTCCCTG	26	O	1919
1486246	20475	20490	22541	22556	CTCTTATTACTACCTT	22	O	1920
1486299	40732	40747	42798	42813	ATGGATGACATTTGTC	39	O	1921
1486332	40319	40334	42385	42400	CTATTTTTCTTGACCC	53	O	1922
1486375	38653	38668	40719	40734	GAAAGCTAAACTACCG	69	O	1923
1486388	33154	33169	35220	35235	GAATTCAGCCACACC	44	O	1924
1486390	25946	25961	28012	28027	TCAAACCTTCTAGCACT	44	O	1925
1486394	39138	39153	41204	41219	ATACTAGATACCAGGG	33	O	1926
1486426	18398	18413	20464	20479	AATTTTGTACATCAC	20	O	1927
1486451	28439	28454	30505	30520	AACATACAACATATGAC	57	O	1928
1486465	18916	18931	20982	20997	GAGCAAACATTCTTTC	28	O	1929
1486466	22013	22028	24079	24094	AAAGTAGATTTTAGGC	17	O	1930
1486487	23185	23200	25251	25266	AACGTACACTGAAAGG	23	O	1931
1486497	36543	36558	38609	38624	TACCTTATAAGTAAGC	27	O	1932
1486513	48477	48492	50543	50558	TGTACTAGTTATTCTC	37	O	1933
1486565	20862	20877	22928	22943	TTTATGTACCATTAGT	36	O	1934
1486588	36016	36031	38082	38097	CCCCATAAATCTTACA	62	O	1935
1486629	17892	17907	19958	19973	CCGTGAAAAGGGTCGG	66	O	1936
1486655	43406	43421	45472	45487	AACTCCATATTGCCAT	38	O	1937
1482568	20497	20512	22563	22578	AATATTTCTCCAGTCC	28	P	1938
1482675	48854	48869	50920	50935	TCATCAATATCTGCAA	36	P	1939
1482763	15815	15830	17881	17896	GTATCTACACATGCCA	41	P	1940
1482834	2663	2678	4729	4744	CTTTGAAAGTCCTTTC	48	P	1941
1482873	44894	44909	46960	46975	GATATCAACATGCCAT	29	P	1942
1483012	31101	31116	33167	33182	ATATCAATTGATTCCC	50	P	1943
1483079	2633	2648	4699	4714	GGCTAATGAATTCCTT	30	P	1944

1483323	47770	47785	49836	49851	GTAGTATAGTCATTGA	23	P	1945
1483355	28486	28501	30552	30567	AGATCTAAACAACCAA	41	P	1946
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	17	P	19
1483886	27426	27441	29492	29507	GATACCATAACAACCAA	29	P	1947
1483923	21484	21499	23550	23565	GATGTATAGTCATGCA	14	P	1948
1483995	32480	32495	34546	34561	GCTCATTTATGTTCTG	23	P	1949
1484592	37717	37732	39783	39798	CAGATATATTCCTGAG	41	P	1950
1484629	18959	18974	21025	21040	CTACTTGTCACATCCC	26	P	1951
1484638	74620	74635	76686	76701	TTCGATTCAAGAACAT	53	P	1952
1484664	98468	98483	100534	100549	TATTACGCTGGGCTAC	67	P	1953
1484724	40767	40782	42833	42848	CTCTACCTCCAGCAAG	69	P	1954
1484747	20864	20879	22930	22945	AGTTTATGTACCATTA	12	P	1955
1484792	21245	21260	23311	23326	GGATATATACTTGTA	12	P	1956
1484893	16506	16521	18572	18587	CTGTTATGTAATATGC	15	P	1957
1484942	32831	32846	34897	34912	CGCATTATCATGGTTG	22	P	1958
1484988	88988	89003	91054	91069	CCGTAGCTATAGTGCA	60	P	1959
1484994	86099	86114	88165	88180	AATTCAAGACTCCTTG	44	P	1960
1485008	25591	25606	27657	27672	ATCAATTCTAAATTCC	16	P	1961
1485038	40321	40336	42387	42402	AGCTATTTTTCTTGAC	63	P	1962
1485056	37985	38000	40051	40066	TGCAAACCTATAGCCTT	41	P	1963
1485066	87317	87332	89383	89398	AAAACCTATACTTGAGC	52	P	1964
1485091	39859	39874	41925	41940	TACCGTCGTTAAACTG	43	P	1965
1485112	36545	36560	38611	38626	CATACCTTATAAGTAA	38	P	1966
1485165	26243	26258	28309	28324	GAATGAGAGTTCTCCA	34	P	1967
1485301	70898	70913	72964	72979	CACGTAGTTACCCACT	48	P	1968
1485312	39682	39697	41748	41763	GAATTAATTGTCTTGA	25	P	1969
1485338	44282	44297	46348	46363	GAAGATGACCCATTGA	48	P	1970
1485361	15482	15497	17548	17563	ACACAATACATACTTC	56	P	1971
1485423	24718	24733	26784	26799	AATCTACTTAGACCTG	35	P	1972
1485424	30529	30544	32595	32610	TCAATAACCATGAGAA	47	P	1973
1485484	19424	19439	21490	21505	AGGTATGAACCTCAAG	12	P	1974
1485492	22029	22044	24095	24110	CTGGTAATTTTCAAG	33	P	1975
1485509	43408	43423	45474	45489	GAAACTCCATATTGCC	14	P	1976
1485512	36094	36109	38160	38175	GAAACATTAAGTGCTT	27	P	1977
1485550	45142	45157	47208	47223	CGTTATACTTATTTTC	34	P	1978
1485559	27997	28012	30063	30078	GTCGAAATTCATGTGA	14	P	1979
1485571	30063	30078	32129	32144	TATTAGAATACCCTCA	69	P	1980
1485592	83502	83517	85568	85583	GCAACTTCAATTTGTG	29	P	1981
1485623	24012	24027	26078	26093	ACTGTATAATGCACTA	23	P	1982
1485631	49069	49084	51135	51150	TATTACAAATAGCTTG	25	P	1983
1485644	25947	25962	28013	28028	ATCAAACCTTCTAGCAC	48	P	1984
1485674	86570	86585	88636	88651	GAGATTAATTAACATT	46	P	1985
1485768	48513	48528	50579	50594	TTCCCAAGAGACCCAG	50	P	1986

1485845	18402	18417	20468	20483	GATTAATTTTGT CACA	31	P	1987
1485864	22546	22561	24612	24627	ATCTAACTCTCATACA	64	P	1988
1485866	33805	33820	35871	35886	TGTAATAGCCTTTATG	43	P	1989
1486047	105089	105104	107155	107170	ACTCTATCACATTCGT	31	P	1990
1486076	31784	31799	33850	33865	GACATATTCAGAATTC	38	P	1991
1486084	72021	72036	74087	74102	ATCCTATTTCAAGTTA	36	P	1992
1486085	35123	35138	37189	37204	GTCCTAAACATGCCAT	45	P	1993
1486129	71305	71320	73371	73386	ATAGATATGACCTGTT	56	P	1994
1486153	67402	67417	69468	69483	GTTTATTCACACTCGG	17	P	1995
1486194	53507	53522	55573	55588	GACTATCAATCGGTAC	27	P	1996
1486196	17903	17918	19969	19984	CTTCTATTAGCCCGTG	32	P	1997
1486214	36991	37006	39057	39072	TTCGTAATTAGTCCCT	24	P	1998
1486216	29274	29289	31340	31355	GGGATAACTTTTTGGA	32	P	1999
1486228	23566	23581	25632	25647	AGATATAGACCATCTC	48	P	2000
1486308	46517	46532	48583	48598	TTTGTAATAGAATAGC	21	P	2001
1486313	45547	45562	47613	47628	CGTACATCATTTGTTA	28	P	2002
1486393	17360	17375	19426	19441	GATTATAAAAGACCCA	18	P	2003
1486423	41836	41851	43902	43917	TCAGATCATAATCAAT	37	P	2004
1486445	41412	41427	43478	43493	TTAACTATATTGAGGT	17	P	2005
1486446	27154	27169	29220	29235	GATAGATAGACTCCTA	35	P	2006
1486498	46285	46300	48351	48366	ACCAACTTTCTTTACA	58	P	2007
1486548	33155	33170	35221	35236	AGAATTCAAGCCACAC	28	P	2008
1486596	43770	43785	45836	45851	ACTTAATACATGTTCC	46	P	2009
1486617	33975	33990	36041	36056	TGATACAAACCTTTCA	53	P	2010
1486641	23188	23203	25254	25269	CGTAACGTACACTGAA	16	P	2011
1486674	19974	19989	22040	22055	CATCGCTGAACCTGGA	30	P	2012
1486685	38671	38686	40737	40752	TTAAAGTTAACCAGGA	49	P	2013
1486695	39139	39154	41205	41220	TATACTAGATACCAGG	39	P	2014

Table 4

3-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1482316	48857	48872	50923	50938	TTTTCATCAATATCTG	23	Q	2015
1482355	28519	28534	30585	30600	TCTCCTAAAGCCTTCA	52	Q	2016
1482534	44897	44912	46963	46978	ATTGATATCAACATGC	24	Q	2017
1482781	2635	2650	4701	4716	ATGGCTAATGAATTCC	32	Q	2018
1483453	30622	30637	32688	32703	ACATTTTCATAGCTGTC	18	Q	2019
1483747	37997	38012	40063	40078	GCTATATCACTATGCA	85	Q	2020
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	16	Q	19
1483933	2665	2680	4731	4746	GCCTTTGAAAGTCCTT	35	Q	2021

1483983	28009	28024	30075	30090	GCAACTAGTATGGTCG	19	Q	2022
1484578	24064	24079	26130	26145	ATGTATCGACACACTT	27	Q	2023
1484614	53780	53795	55846	55861	AGTACAACACTGCCAT	30	Q	2024
1484666	72067	72082	74133	74148	AATTTTAAACCAACTC	75	Q	2025
1484673	40358	40373	42424	42439	TTAACTCCTATGCCGT	32	Q	2026
1484719	45144	45159	47210	47225	TACGTTATACTTATTT	43	Q	2027
1484759	68077	68092	70143	70158	GATATTCCAAAACCTGC	37	Q	2028
1484844	21524	21539	23590	23605	AAAACATCATCGCAA	48	Q	2029
1484868	25952	25967	28018	28033	CTATGATCAAACCTTCT	87	Q	2030
1484917	98470	98485	100536	100551	AATATTACGCTGGGCT	76	Q	2031
1484923	47819	47834	49885	49900	CAGCATATCCTATGGA	34	Q	2032
1484983	86102	86117	88168	88183	TTAAATTCAAGACTCC	55	Q	2033
1484992	29276	29291	31342	31357	TAGGGATAACTTTTTG	53	Q	2034
1484997	49076	49091	51142	51157	CCCTGAATATTCACAA	67	Q	2035
1485014	40813	40828	42879	42894	TCTAACACCATCTTGG	73	Q	2036
1485031	41842	41857	43908	43923	AGAAGATCAGATCATA	79	Q	2037
1485152	18981	18996	21047	21062	ACAAGCTAGACATCCA	25	Q	2038
1485168	15910	15925	17976	17991	GGTACAAATAAAGAGC	105	Q	2039
1485180	23568	23583	25634	25649	GCAGATATAGACCATC	26	Q	2040
1485191	20894	20909	22960	22975	GCCATAATAATTGTGT	30	Q	2041
1485196	37008	37023	39074	39089	CTAACCCGGTCTAAAC	84	Q	2042
1485233	31104	31119	33170	33185	AGGATATCAATTGATT	22	Q	2043
1485328	19426	19441	21492	21507	AAAGGTATGAACCTCA	20	Q	2044
1485331	30066	30081	32132	32147	GTTTATTAGAATACCC	18	Q	2045
1485397	26262	26277	28328	28343	CTTGTAACATCCTAC	34	Q	2046
1485417	44309	44324	46375	46390	ACATATCCAAGGGCCC	54	Q	2047
1485425	83530	83545	85596	85611	ATCCATTTAGACTCCA	42	Q	2048
1485459	48553	48568	50619	50634	ATTATTAATACACCTC	35	Q	2049
1485465	41495	41510	43561	43576	AGGTAATTAAGTTTTG	23	Q	2050
1485485	87413	87428	89479	89494	CTTACCAGCTTATTGG	62	Q	2051
1485499	71350	71365	73416	73431	TCTAATAGCATCTCTA	49	Q	2052
1485525	37719	37734	39785	39800	ATCAGATATATTCCTG	67	Q	2053
1485543	36126	36141	38192	38207	CATATCTTATGTACAT	27	Q	2054
1485544	33980	33995	36046	36061	ACAAATGATACAAACC	67	Q	2055
1485588	39749	39764	41815	41830	TCATATGCTTTACTAT	49	Q	2056
1485752	43442	43457	45508	45523	TAAGACTTCTCCTTCA	67	Q	2057
1485799	24752	24767	26818	26833	GCTGAGATCATTTCATC	88	Q	2058
1485888	46539	46554	48605	48620	GATATCTCATACATTT	22	Q	2059
1485896	39186	39201	41252	41267	GTGTAGAGATCAACAG	79	Q	2060
1485918	22214	22229	24280	24295	TCCTATTTATGCCCGT	24	Q	2061
1485930	39862	39877	41928	41943	CATTACCGTCGTAAA	75	Q	2062
1485933	88990	89005	91056	91071	CGCCGTAGCTATAGTG	56	Q	2063
1485939	21321	21336	23387	23402	CACAATTTAATGTATG	57	Q	2064

1485947	27434	27449	29500	29515	TAGTACTGGATACCAT	18	Q	2065
1485958	32869	32884	34935	34950	TCAAGATAAAATTTGCG	78	Q	2066
1485975	25607	25622	27673	27688	GGGTAAAAAACCATGT	45	Q	2067
1486010	36571	36586	38637	38652	GTATAACTGTCTCAGT	29	Q	2068
1486024	20584	20599	22650	22665	GACAAGAACCAAACCTT	48	Q	2069
1486031	15494	15509	17560	17575	ACCTTCTAAGCAACAC	57	Q	2070
1486041	17966	17981	20032	20047	CCATTAAGCTCTTTGA	31	Q	2071
1486112	70920	70935	72986	73001	TTAACACATCCATTGT	70	Q	2072
1486113	18440	18455	20506	20521	AAGAACTATACTACC	77	Q	2073
1486192	27157	27172	29223	29238	ATTGATAGATAGACTC	22	Q	2074
1486284	43811	43826	45877	45892	ATTCCTTAACCTACAG	63	Q	2075
1486293	22554	22569	24620	24635	GATGTATCATCTAACT	40	Q	2076
1486294	86640	86655	88706	88721	GAAGTTAACTCCCTAG	46	Q	2077
1486360	38674	38689	40740	40755	CAGTTAAAGTTAACCA	18	Q	2078
1486377	32512	32527	34578	34593	ATGTAAATAGAACCTA	72	Q	2079
1486404	17362	17377	19428	19443	ATGATTATAAAAGACC	25	Q	2080
1486405	33157	33172	35223	35238	CTAGAATTCAAGCCAC	43	Q	2081
1486439	23190	23205	25256	25271	ACCGTAACGTACACTG	24	Q	2082
1486461	33824	33839	35890	35905	ATATGATACACCTGGA	55	Q	2083
1486512	74625	74640	76691	76706	GGATATTCGATTCAAG	45	Q	2084
1486546	19985	20000	22051	22066	ACAATAAATAACATCG	34	Q	2085
1486555	105441	105456	107507	107522	CCAATTGCAACCCCAA	67	Q	2086
1486564	31941	31956	34007	34022	AATGTATCTCTAACAA	73	Q	2087
1486600	46289	46304	48355	48370	ACCTACCAACTTTCTT	66	Q	2088
1486644	16577	16592	18643	18658	TCAAACTATATCTCT	53	Q	2089
1486667	35153	35168	37219	37234	CATGACAGTATCATAG	71	Q	2090
1486709	45549	45564	47615	47630	CACGTACATCATTTGT	48	Q	2091
1482145	2666	2681	4732	4747	GGCCTTTGAAAGTCCT	33	R	2092
1482184	48858	48873	50924	50939	GTTTTCATCAATATCT	15	R	2093
1482685	30623	30638	32689	32704	TACATTTCATAGCTGT	33	R	2094
1482715	36573	36588	38639	38654	ATGTATAACTGTCTCA	12	R	2095
1483512	33825	33840	35891	35906	CATATGATACACCTGG	26	R	2096
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	18	R	19
1483897	15495	15510	17561	17576	CACCTTCTAAGCAACA	62	R	2097
1483984	21526	21541	23592	23607	ACAAACTATCATCGC	12	R	2098
1484203	44899	44914	46965	46980	GTATTGATATCAACAT	32	R	2099
1484353	2636	2651	4702	4717	CATGGCTAATGAATTC	59	R	2100
1484481	88996	89011	91062	91077	TCTTATCGCCGTAGCT	57	R	2101
1484485	87420	87435	89486	89501	AACCAGTCTTACCAGC	35	R	2102
1484511	47851	47866	49917	49932	CAGGAGACACAACCTGA	100	R	2103
1484542	38675	38690	40741	40756	GCAGTTAAAGTTAACC	8	R	2104
1484566	25608	25623	27674	27689	CGGGTTAAAAACCATG	23	R	2105
1484572	27442	27457	29508	29523	CTATCTAATAGTACTG	27	R	2106

1484573	41521	41536	43587	43602	AAGTACCTTCTGCTCT	45	R	2107
1484685	30067	30082	32133	32148	AGTTTATTAGAATACC	33	R	2108
1484688	40814	40829	42880	42895	TTCTAACACCATCTTG	66	R	2109
1484693	37721	37736	39787	39802	CTATCAGATATATTCC	30	R	2110
1484700	19451	19466	21517	21532	TTAACCTGTTTCTACT	61	R	2111
1484767	74754	74769	76820	76835	TAAGCTTATGACTTGC	23	R	2112
1484825	27241	27256	29307	29322	GATACTTCACTCAGAA	26	R	2113
1484871	24065	24080	26131	26146	CATGTATCGACACACT	26	R	2114
1484907	46290	46305	48356	48371	TACCTACCAACTTTCT	63	R	2115
1484941	17377	17392	19443	19458	TCTTATACTAAGCATA	30	R	2116
1484989	106025	106040	108091	108106	CTACGTGATCCGAATT	71	R	2117
1484996	37998	38013	40064	40079	GGCTATATCACTATGC	33	R	2118
1485049	70942	70957	73008	73023	AAGGTTATTATAGTGA	19	R	2119
1485055	20623	20638	22689	22704	CTAATAGTCATCTGGT	40	R	2120
1485146	21344	21359	23410	23425	TAATTTTCAGTCTACTG	28	R	2121
1485201	43814	43829	45880	45895	AATATTCCTTAACCTA	48	R	2122
1485284	43463	43478	45529	45544	GGAGATATAGACTTAA	32	R	2123
1485306	71352	71367	73418	73433	GATCTAATAGCATCTC	17	R	2124
1485435	53783	53798	55849	55864	CTAAGTACAACACTGC	47	R	2125
1485468	32870	32885	34936	34951	ATCAAGATAAATTTGC	79	R	2126
1485523	20896	20911	22962	22977	AGGCCATAATAATTGT	51	R	2127
1485575	39751	39766	41817	41832	ACTCATATGCTTTACT	74	R	2128
1485633	46540	46555	48606	48621	TGATATCTCATACATT	27	R	2129
1485636	36127	36142	38193	38208	GCATATCTTATGTACA	10	R	2130
1485647	24851	24866	26917	26932	CCATTCTAAAAAGTTC	27	R	2131
1485668	86643	86658	88709	88724	GATGAAGTTAACTCCC	36	R	2132
	87648	87663	89714	89729				
1485705	83549	83564	85615	85630	CGAATAATAAGATTCA	60	R	2133
1485719	26294	26309	28360	28375	GCCTACTGGCGTTAAA	84	R	2134
1485746	28559	28574	30625	30640	GATATTTATCACATGA	7	R	2135
1485747	32565	32580	34631	34646	GCACAGAAATTCATTA	20	R	2136
1485758	22215	22230	24281	24296	ATCCTATTTATGCCCCG	14	R	2137
1485763	72105	72120	74171	74186	GATTAGTTCTTCCCTC	37	R	2138
1485792	15948	15963	18014	18029	CAACATTTGTCACTTG	46	R	2139
1485865	31962	31977	34028	34043	CCAATAAAATGCCTAG	37	R	2140
1485915	45550	45565	47616	47631	ACACGTACATCATTTG	18	R	2141
1485917	18497	18512	20563	20578	CACAACATGCTGCAA	22	R	2142
1485972	22555	22570	24621	24636	AGATGTATCATCTAAC	22	R	2143
1485983	29313	29328	31379	31394	GAAATTTACATAGTG	25	R	2144
1486059	23569	23584	25635	25650	AGCAGATATAGACCAT	26	R	2145
1486072	39252	39267	41318	41333	GGCTAGCTACTTTTGA	59	R	2146
1486144	69073	69088	71139	71154	GCTGATTTATTGATGG	43	R	2147
1486145	37043	37058	39109	39124	CATCCTAAAGTATTGC	25	R	2148

1486149	17967	17982	20033	20048	CCCATTAAGCTCTTTG	30	R	2149
1486156	33985	34000	36051	36066	GACATACAAATGATAC	19	R	2150
1486182	86121	86136	88187	88202	AAGATAGACACTTCAC	33	R	2151
1486211	35215	35230	37281	37296	TAGAATTCACCTCTGTA	34	R	2152
1486281	28071	28086	30137	30152	TGGATAAAGTACATTA	23	R	2153
1486286	98915	98930	100981	100996	TAAGTTTTGTCACAGT	33	R	2154
1486291	41862	41877	43928	43943	GAGGATCAAATTTAGG	77	R	2155
1486304	23191	23206	25257	25272	TACCGTAACGTACACT	27	R	2156
1486323	40359	40374	42425	42440	CTTAACCTCTATGCCG	36	R	2157
1486373	25953	25968	28019	28034	CCTATGATCAAACCTC	57	R	2158
1486374	48566	48581	50632	50647	ACTATAACACTGCATT	42	R	2159
1486418	19996	20011	22062	22077	GATTTTGAACAACAAT	64	R	2160
1486420	18984	18999	21050	21065	TCTACAAGCTAGACAT	47	R	2161
1486438	16578	16593	18644	18659	CTCAAACTATATCTC	34	R	2162
1486482	49108	49123	51174	51189	GTATAAGATTCTCTGCT	46	R	2163
1486550	33205	33220	35271	35286	CACATTATATATCCTT	38	R	2164
1486554	39863	39878	41929	41944	TCATTACCGTCGTTAA	37	R	2165
1486616	44331	44346	46397	46412	CATACTCACAGCAGTC	35	R	2166
1486693	45148	45163	47214	47229	CCTATACGTTATACTT	23	R	2167
1486710	31135	31150	33201	33216	AGCTAATGGCCCTTCC	47	R	2168
1482231	2667	2682	4733	4748	TGGCCTTTGAAAGTCC	39	S	2169
1482400	43856	43871	45922	45937	GCATTTATCATCTTGA	13	S	2170
1482446	2637	2652	4703	4718	CCATGGCTAATGAATT	33	S	2171
1483336	40819	40834	42885	42900	TGTAATTCTAACACCA	30	S	2172
1483549	18998	19013	21064	21079	GCCATTAATCCACTTC	25	S	2173
1483637	27443	27458	29509	29524	ACTATCTAATAGTACT	46	S	2174
1483812	48859	48874	50925	50940	GGTTTTTCATCAATATC	10	S	2175
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	20	S	19
1484177	33826	33841	35892	35907	TCATATGATACACCTG	35	S	2176
1484278	21346	21361	23412	23427	GGTAATTTTCAGTCTAC	20	S	2177
1484493	47906	47921	49972	49987	CTGCTATTAACGATTT	22	S	2178
1484555	24117	24132	26183	26198	CTTACTTAATATCATC	27	S	2179
1484627	38012	38027	40078	40093	TTACTATCTTACGTGG	44	S	2180
1484684	30624	30639	32690	32705	GTACATTTTCATAGCTG	22	S	2181
1484735	87426	87441	89492	89507	CCTTTAAACCAGTCTT	39	S	2182
1484755	106027	106042	108093	108108	CCCTACGTGATCCGAA	54	S	2183
1484773	32576	32591	34642	34657	TATATGGCACTGCACA	45	S	2184
1484788	39755	39770	41821	41836	AACTACTCATATGCTT	49	S	2185
1484824	44916	44931	46982	46997	TCATATGTAAACTTGG	26	S	2186
1484828	53905	53920	55971	55986	AACACCGGGACTGGCG	36	S	2187
1484913	83612	83627	85678	85693	GCTGAATCAGACGGGT	35	S	2188
1484926	48567	48582	50633	50648	AACTATAACACTGCAT	40	S	2189
1484934	22578	22593	24644	24659	GTAGAAGAACAATTAA	40	S	2190

1484951	26353	26368	28419	28434	AAATTCCTCAAGGGC	22	S	2191
1484965	38723	38738	40789	40804	CAGTTAAATACGTTTG	31	S	2192
1484967	19455	19470	21521	21536	ACTTTTAACCTGTTTC	52	S	2193
1485121	44332	44347	46398	46413	ACATACTCACAGCAGT	41	S	2194
1485182	15507	15522	17573	17588	TAATTTCCACCACACC	59	S	2195
1485254	21527	21542	23593	23608	AACAAAACATCATCG	64	S	2196
1485274	37088	37103	39154	39169	TTTAGTTCATTTTGGC	20	S	2197
1485279	86675	86690	88741	88756	TCGTATACAGCGTCTA	52	S	2198
1485293	25618	25633	27684	27699	AATACGTCCGCGGGTT	23	S	2199
1485297	71358	71373	73424	73439	GAAGTTGATCTAATAG	30	S	2200
1485304	72106	72121	74172	74187	AGATTAGTTCTTCCCT	33	S	2201
1485305	45149	45164	47215	47230	TCCTATACGTTATACT	70	S	2202
1485343	16611	16626	18677	18692	AGTCAAAATTCTTCTC	27	S	2203
1485348	28072	28087	30138	30153	GTGGATAAAGTACATT	32	S	2204
1485353	20624	20639	22690	22705	CCTAATAGTCATCTGG	44	S	2205
1485355	41991	42006	44057	44072	TAGAGATGAATTCCAG	49	S	2206
1485426	23570	23585	25636	25651	CAGCAGATATAGACCA	39	S	2207
1485472	31963	31978	34029	34044	CCCAATAAAATGCCTA	39	S	2208
1485530	36142	36157	38208	38223	CTAATTGCATTCCTGG	42	S	2209
1485563	49109	49124	51175	51190	GGTATAAGATTCCTGC	19	S	2210
1485569	33206	33221	35272	35287	CCACATTATATATCCT	14	S	2211
1485583	27242	27257	29308	29323	TGATACTTCACTCAGA	28	S	2212
1485672	37732	37747	39798	39813	TCCATAAAACACTATC	18	S	2213
1485735	23194	23209	25260	25275	AAATACCGTAACGTAC	47	S	2214
1485766	25954	25969	28020	28035	CCCTATGATCAAACCTT	61	S	2215
1485780	46291	46306	48357	48372	GTACCTACCAACTTTC	45	S	2216
1485797	31137	31152	33203	33218	GAAGCTAATGGCCCTT	25	S	2217
1485890	18011	18026	20077	20092	ACAATCAGAAGATTGA	92	S	2218
1485996	69519	69534	71585	71600	CTGGTATCGAACAGCC	43	S	2219
1486016	28690	28705	30756	30771	ACCAATTAGTTTCTAA	19	S	2220
1486053	40360	40375	42426	42441	TCTTAACTCCTATGCC	47	S	2221
1486091	39881	39896	41947	41962	TAATCAAGCTGCCCTC	79	S	2222
1486131	29327	29342	31393	31408	TAGGAGACCAAAGTGA	44	S	2223
1486179	22216	22231	24282	24297	TATCCTATTTATGCCC	33	S	2224
1486184	20935	20950	23001	23016	CCATCTTGAACCCAGT	21	S	2225
1486225	36574	36589	38640	38655	AATGTATAACTGTCTC	23	S	2226
1486235	43464	43479	45530	45545	CGGAGATATAGACTTA	20	S	2227
1486282	19999	20014	22065	22080	TCTGATTTTGAACAAC	16	S	2228
1486298	98938	98953	101004	101019	TATCTTGTAATTCTC	45	S	2229
1486380	15951	15966	18017	18032	CTCCAACATTTGTCAC	79	S	2230
1486397	41522	41537	43588	43603	AAAGTACCTTCTGCTC	73	S	2231
1486463	45553	45568	47619	47634	CTTACACGTACATCAT	21	S	2232
1486474	17378	17393	19444	19459	TTCTTATACTAAGCAT	25	S	2233

1486476	33987	34002	36053	36068	GTGACATACAAATGAT	31	S	2234
1486503	86122	86137	88188	88203	TAAGATAGACACTTCA	103	S	2235
1486540	70943	70958	73009	73024	AAAGGTTATTATAGTG	25	S	2236
1486556	46682	46697	48748	48763	ATCACGACATTTTCTT	62	S	2237
1486557	30068	30083	32134	32149	AAGTTTATTAGAATAC	58	S	2238
1486589	74761	74776	76827	76842	GCGATACTAAGCTTAT	129	S	2239
1486631	18498	18513	20564	20579	CCACAACATATGCTGCA	28	S	2240
1486659	32878	32893	34944	34959	GATAGAATATCAAGAT	31	S	2241
1486661	39266	39281	41332	41347	TATATCTCAACTCAGG	40	S	2242
1486669	35239	35254	37305	37320	ACAACATAAGTCCATA	27	S	2243
1486678	24936	24951	27002	27017	CAGATAAACCATCCCA	47	S	2244
1486707	88997	89012	91063	91078	CTCTTATCGCCGTAGC	37	S	2245
1482155	19457	19472	21523	21538	GCACTTTAACTTGT	39	T	2246
1482197	15508	15523	17574	17589	TTAATTTCCACCACAC	66	T	2247
1482218	24937	24952	27003	27018	GCAGATAAACCATCCC	44	T	2248
1482330	48860	48875	50926	50941	AGGTTTTCATCAATAT	58	T	2249
1482459	27451	27466	29517	29532	TCTGATTTACTATCTA	53	T	2250
1482508	31171	31186	33237	33252	AAGAGTAAACACAGGC	51	T	2251
1483459	2638	2653	4704	4719	TCCATGGCTAATGAAT	67	T	2252
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	16	T	19
1484010	2668	2683	4734	4749	TTGGCCTTTGAAAGTC	70	T	2253
1484228	17411	17426	19477	19492	TGATTGTAACCTTTGG	52	T	2254
1484538	15971	15986	18037	18052	CACACCCGTCACCACT	99	T	2255
1484628	42333	42348	44399	44414	GCAATTATCTACTTAA	46	T	2256
1484698	39267	39282	41333	41348	CTATATCTCAACTCAG	73	T	2257
1484808	32577	32592	34643	34658	GTATATGGCACTGCAC	86	T	2258
1484817	74776	74791	76842	76857	CTTAGTATCACATTGG	96	T	2259
1484833	32879	32894	34945	34960	GGATAGAATATCAAGA	46	T	2260
1484940	49110	49125	51176	51191	AGGTATAAGATTCTTG	80	T	2261
1484950	54770	54785	56836	56851	AATGATCTATGATCCA	31	T	2262
1484971	37764	37779	39830	39845	TATTACTCACTCCAGG	72	T	2263
1484980	72107	72122	74173	74188	GAGATTAGTTCTTCCC	59	T	2264
1485023	34286	34301	36352	36367	TACTGTACCATTTTGT	69	T	2265
1485039	106028	106043	108094	108109	GCCCTACGTGATCCGA	86	T	2266
1485057	69978	69993	72044	72059	CCGTACTATTGTCCAT	65	T	2267
1485070	44917	44932	46983	46998	CTCATATGTAAACTTG	51	T	2268
1485264	40820	40835	42886	42901	TTGTAATTCTAACACC	80	T	2269
1485268	20008	20023	22074	22089	GAACCTCATTCTGATT	45	T	2270
1485289	38724	38739	40790	40805	CCAGTTAAATACGTTT	66	T	2271
1485291	28102	28117	30168	30183	TTAACAAAAGTATCGA	78	T	2272
1485311	43858	43873	45924	45939	TCGCATTTATCATCTT	59	T	2273
1485333	29346	29361	31412	31427	ATGGTATATCTGCAAA	77	T	2274
1485378	33827	33842	35893	35908	ATCATATGATACACCT	62	T	2275

1485430	44333	44348	46399	46414	TACATACTCACAGCAG	72	T	2276
1485457	21564	21579	23630	23645	TTCTATCCCACTCATC	94	T	2277
1485497	18039	18054	20105	20120	CTCTGTAGATTTCTGT	96	T	2278
1485503	30632	30647	32698	32713	AACGTACTGTACATTT	58	T	2279
1485518	39885	39900	41951	41966	CCTGTAATCAAGCTGC	13	T	2280
1485528	83761	83776	85827	85842	AGTTTTTCATCAAGTGC	50	T	2281
1485535	47914	47929	49980	49995	GTATACAGCTGCTATT	82	T	2282
1485609	46292	46307	48358	48373	AGTACCTACCAACTTT	100	T	2283
1485673	28735	28750	30801	30816	CTTATATATACACGTT	61	T	2284
1485675	26354	26369	28420	28435	AAAATTTCTCAAGGG	91	T	2285
1485680	23196	23211	25262	25277	TGAAATACCGTAACGT	63	T	2286
1485699	23623	23638	25689	25704	AACCACGAGCCGTCAT	60	T	2287
1485833	86680	86695	88746	88761	GCTTTTCGTATACAGC	93	T	2288
1485849	40368	40383	42434	42449	ATCTATGCTCTTAACT	68	T	2289
1485850	27244	27259	29310	29325	TATGATACTTCACTCA	66	T	2290
1485859	22252	22267	24318	24333	GAGACAAGATATATGG	55	T	2291
1485882	99231	99246	101297	101312	CTTCAAGATCGGTGGA	77	T	2292
1485911	33245	33260	35311	35326	GATAGTATTTTCCTAT	72	T	2293
1485957	39757	39772	41823	41838	TTAACTACTCATATGC	108	T	2294
1485970	38013	38028	40079	40094	TTTACTATCTTACGTG	80	T	2295
1485974	20945	20960	23011	23026	CACTATTCATCCATCT	70	T	2296
1485976	20627	20642	22693	22708	ATACCTAATAGTCATC	66	T	2297
1485977	87427	87442	89493	89508	TCCTTTAAACCAGTCT	70	T	2298
1486018	25619	25634	27685	27700	GAATACGTCCGCGGGT	63	T	2299
1486023	31978	31993	34044	34059	CATACTAACTTCTCTC	70	T	2300
1486033	35240	35255	37306	37321	TACAACATAAAGTCCAT	78	T	2301
1486115	36577	36592	38643	38658	AGTAATGTATAACTGT	65	T	2302
1486150	18513	18528	20579	20594	GTCCAATGTTTATTTT	54	T	2303
1486151	86123	86138	88189	88204	CTAAGATAGACACTTC	83	T	2304
1486152	71395	71410	73461	73476	GAGTAACTGTTCCATA	57	T	2305
1486154	70982	70997	73048	73063	GTAAACAACATGCTGT	80	T	2306
1486155	37107	37122	39173	39188	ATGGTAATCTCCCTGT	61	T	2307
1486173	46683	46698	48749	48764	CATCACGACATTTTCT	77	T	2308
1486177	48569	48584	50635	50650	GAAACTATAAACAATGC	62	T	2309
1486198	36143	36158	38209	38224	CCTAATTGCATTCCTG	68	T	2310
1486209	24233	24248	26299	26314	ATGGAATCACATGACT	67	T	2311
1486344	25979	25994	28045	28060	TCAACCATAATGCATT	69	T	2312
1486351	89595	89610	91661	91676	GATGATACATCTTCTT	61	T	2313
1486398	41523	41538	43589	43604	CAAAGTACCTTCTGCT	77	T	2314
1486419	43465	43480	45531	45546	ACGGAGATATAGACTT	60	T	2315
1486460	21347	21362	23413	23428	AGGTAATTTTCAGTCTA	63	T	2316
1486475	45571	45586	47637	47652	GAAATTTTCTTACATC	68	T	2317
1486490	22579	22594	24645	24660	TGTAGAAGAACAATTA	74	T	2318

1486519	30087	30102	32153	32168	AAGTATACAGCATAGA	60	T	2319
1486618	45334	45349	47400	47415	TACTGAATTACCACAA	89	T	2320
1486648	16653	16668	18719	18734	TGGTATAATCTTATTC	49	T	2321
1486696	19003	19018	21069	21084	GCAGAGCCATTAATCC	31	T	2322
1482636	21348	21363	23414	23429	GAGGTAATTTTCAGTCT	24	U	2323
1482814	2639	2654	4705	4720	ATCCATGGCTAATGAA	21	U	2324
1482976	39268	39283	41334	41349	CCTATATCTCAACTCA	46	U	2325
1483189	2671	2686	4737	4752	TCCTTGGCCTTTGAAA	72	U	2326
1483376	31216	31231	33282	33297	AACGATTTCACTGGCA	14	U	2327
1483492	15509	15524	17575	17590	GTTAATTTCCACCACA	58	U	2328
1483695	45336	45351	47402	47417	CCTACTGAATTACCAC	40	U	2329
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	25	U	19
1484214	43870	43885	45936	45951	TTTTAGTTCTCATCGC	11	U	2330
1484307	48861	48876	50927	50942	AAGGTTTTTCATCAATA	10	U	2331
1484510	22255	22270	24321	24336	TTGGAGACAAGATATA	36	U	2332
1484532	38014	38029	40080	40095	GTTTACTATCTTACGT	61	U	2333
1484554	19035	19050	21101	21116	ATTACTCCCTTTCAGT	38	U	2334
1484591	72108	72123	74174	74189	CGAGATTAGTTCTTCC	17	U	2335
1484615	37765	37780	39831	39846	ATATTACTCACTCCAG	53	U	2336
1484617	24938	24953	27004	27019	TGCAGATAAACCATCC	29	U	2337
1484619	100147	100162	102213	102228	CTCGGTTGAATATACT	43	U	2338
1484695	18534	18549	20600	20615	GACTAGCCATTTTCAC	48	U	2339
1484793	24244	24259	26310	26325	CATAATACTCAATGGA	9	U	2340
1484807	35241	35256	37307	37322	TTACAACATAAAGTCCA	25	U	2341
1484862	25980	25995	28046	28061	ATCAACCATAATGCAT	26	U	2342
1484881	17435	17450	19501	19516	CAAGATATTCATCCAA	11	U	2343
1484898	28847	28862	30913	30928	GAAACAACACTACCAT	80	U	2344
1484900	19502	19517	21568	21583	TCTATATAACATCACT	44	U	2345
1484904	23197	23212	25263	25278	ATGAAATACCGTAACG	16	U	2346
1484957	34302	34317	36368	36383	ACCTATCTTCCAAAGT	46	U	2347
1484969	20089	20104	22155	22170	TGTCAATCCATTTGAA	20	U	2348
1485022	39760	39775	41826	41841	ACATTAACACTACTATA	45	U	2349
1485027	27476	27491	29542	29557	CGTCTAAAATTTTTGT	18	U	2350
1485061	23625	23640	25691	25706	TAAACCACGAGCCGTC	39	U	2351
1485080	32882	32897	34948	34963	ACTGGATAGAATATCA	30	U	2352
1485155	87428	87443	89494	89509	TTCTTTTAAACCAGTC	20	U	2353
1485158	33255	33270	35321	35336	AGCTAATAATGATAGT	54	U	2354
1485181	41524	41539	43590	43605	ACAAAGTACCTTCTGC	32	U	2355
1485193	21595	21610	23661	23676	TAAACCTATTTGTTGG	22	U	2356
1485296	36144	36159	38210	38225	TCCTAATTGCATTCCT	49	U	2357
1485323	37109	37124	39175	39190	AAATGGTAATCTCCCT	41	U	2358
1485352	44918	44933	46984	46999	TCTCATATGTAAACTT	21	U	2359
1485388	40375	40390	42441	42456	ACTTTAAATCTATGCT	62	U	2360

1485486	30092	30107	32158	32173	ATGATAAGTATACAGC	21	U	2361
1485527	20628	20643	22694	22709	TATACCTAATAGTCAT	35	U	2362
1485537	31979	31994	34045	34060	TCATACTAAGTTCTCT	73	U	2363
1485598	29389	29404	31455	31470	GTTAGATATAAAAGGT	54	U	2364
1485612	46690	46705	48756	48771	CTAGGAACATCACGAC	35	U	2365
1485676	40842	40857	42908	42923	GCAATAAATCTCTTGT	35	U	2366
1485684	89610	89625	91676	91691	TTTACATATGCATTGG	20	U	2367
1485710	30709	30724	32775	32790	CTATATTCCTCAGCGT	20	U	2368
1485773	33828	33843	35894	35909	AATCATATGATACACC	30	U	2369
1485858	16666	16681	18732	18747	GTTATAATATCTTTGG	6	U	2370
1485861	25620	25635	27686	27701	GGAATACGTCCGCGGG	13	U	2371
1485899	20950	20965	23016	23031	GAATTCACCTATTCATC	19	U	2372
1485900	47916	47931	49982	49997	TGGTATACAGCTGCTA	10	U	2373
1485923	70148	70163	72214	72229	ACCAACACATACCTAG	90	U	2374
1485978	49111	49126	51177	51192	GAGGTATAAGATTCCCT	39	U	2375
1485986	18052	18067	20118	20133	GACTACCCACTTCCTC	38	U	2376
1486052	43514	43529	45580	45595	GAAGGTTACTAAAGAG	20	U	2377
1486056	83769	83784	85835	85850	GCTATATAAGTTTTCA	18	U	2378
1486088	71435	71450	73501	73516	GCTGAATTTCTTCAGC	48	U	2379
1486105	86245	86260	88311	88326	GCACTTATTTAGGCAC	37	U	2380
1486180	55231	55246	57297	57312	AGGATTAAACAGTCCA	45	U	2381
1486248	86807	86822	88873	88888	GACAATGTCTATCCAC	23	U	2382
1486261	74875	74890	76941	76956	CGCCCTTACTATATAA	89	U	2383
1486263	42334	42349	44400	44415	TGCAATTATCTACTTA	40	U	2384
1486288	27245	27260	29311	29326	CTATGATACTTCACTC	27	U	2385
1486306	39891	39906	41957	41972	ATAAGACCTGTAATCA	43	U	2386
1486331	48592	48607	50658	50673	AACTTTTTTATTCGTT	57	U	2387
1486339	26370	26385	28436	28451	ATAGTTACTTAGTTGC	3	U	168
1486435	38725	38740	40791	40806	GCCAGTTAAATACGTT	60	U	2388
1486453	28103	28118	30169	30184	GTTAACAAAAGTATCG	21	U	2389
1486455	22620	22635	24686	24701	ATTACTTCATATACGA	8	U	2390
1486456	70983	70998	73049	73064	AGTAAACAACATGCTG	38	U	2391
1486469	46296	46311	48362	48377	ATGGAGTACCTACCAA	95	U	2392
1486502	44334	44349	46400	46415	CTACATACTCACAGCA	39	U	2393
1486507	16041	16056	18107	18122	CCTTTTGTGACAAAGCC	51	U	2394
1486544	45591	45606	47657	47672	AATACCTCCTCTTCAG	42	U	2395
1486551	36616	36631	38682	38697	GAAGAATAGAGATTGT	21	U	2396
1486607	32591	32606	34657	34672	TAGAATTCATAATGGT	22	U	2397
1486672	106414	106429	108480	108495	TCCTATTCTAGAGTCC	35	U	2398
1482427	17436	17451	19502	19517	TCAAGATATTCATCCA	11	V	2399
1482533	2640	2655	4706	4721	CATCCATGGCTAATGA	52	V	2400
1483058	48862	48877	50928	50943	AAAGGTTTTTCATCAAT	12	V	2401
1483067	38754	38769	40820	40835	GACAAATTCAGCTTC	27	V	2402

1483535	38015	38030	40081	40096	AGTTTACTATCTTACG	30	V	2403
1483707	43872	43887	45938	45953	TGTTTTAGTTCTCATC	26	V	2404
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	12	V	19
1484527	46701	46716	48767	48782	TTTAACTTGCACTAGG	40	V	2405
1484694	70268	70283	72334	72349	AGCTTAATATCCTCCA	42	V	2406
1484711	27246	27261	29312	29327	ACTATGATACTTCACT	73	V	2407
1484764	19037	19052	21103	21118	CCATTACTCCCTTCA	34	V	2408
1484778	32592	32607	34658	34673	CTAGAATTCATAATGG	42	V	2409
1484809	20102	20117	22168	22183	CAGAATATACACGTGT	21	V	2410
1484838	15510	15525	17576	17591	AGTTAATTTCCACCAC	44	V	2411
1484918	100153	100168	102219	102234	GATAGACTCGGTTGAA	52	V	2412
1484927	23629	23644	25695	25710	CAGTTAAACCACGAGC	12	V	2413
1484945	33306	33321	35372	35387	TTTATACAGATGATGC	28	V	2414
1484993	70985	71000	73051	73066	ACAGTAAACAACATGC	28	V	2415
1485004	30711	30726	32777	32792	CACTATATTCCTCAGC	45	V	2416
1485086	47939	47954	50005	50020	CTCTACATATTTAGGT	47	V	2417
1485089	18537	18552	20603	20618	GAAGACTAGCCATTTT	71	V	2418
1485111	34312	34327	36378	36393	GAAATTGTCAACCTAT	31	V	2419
1485120	22314	22329	24380	24395	GCAGAAAAGTCAAGTT	27	V	2420
1485138	40854	40869	42920	42935	TAGCTATTGCCTGCAA	48	V	2421
1485217	22711	22726	24777	24792	GATTCCAGAATCACCT	33	V	2422
1485224	106464	106479	108530	108545	CCAATAACTTCATCAA	36	V	2423
1485232	23226	23241	25292	25307	TATGTACAACCTCAGA	24	V	2424
1485234	28848	28863	30914	30929	TGAAACAACACTACCA	44	V	2425
1485259	37766	37781	39832	39847	AATATTACTCACTCCA	51	V	2426
1485272	44335	44350	46401	46416	CCTACATACTCACAGC	42	V	2427
1485302	16071	16086	18137	18152	ACGTACACAGCCATAC	78	V	2428
1485319	44923	44938	46989	47004	TTAAGTCTCATATGTA	25	V	2429
1485322	42553	42568	44619	44634	GTCATAATATTCTTGA	35	V	2430
1485340	19503	19518	21569	21584	CTCTATATAACATCAC	15	V	2431
1485345	31980	31995	34046	34061	ATCATACTAACTTCTC	35	V	2432
1485346	48593	48608	50659	50674	GAACCTTTTTTATTCGT	30	V	2433
1485354	89843	89858	91909	91924	GTAAATTCACATTCCT	23	V	2434
1485442	32897	32912	34963	34978	TCAGTACCAAGTAAGA	26	V	2435
1485526	30093	30108	32159	32174	CATGATAAGTATACAG	26	V	2436
1485551	18077	18092	20143	20158	TATTCCAAATGACTGT	41	V	2437
1485553	36706	36721	38772	38787	CTTTATTATTCTCAGG	17	V	2438
1485566	24245	24260	26311	26326	GCATAATACTCAATGG	21	V	2439
1485589	36167	36182	38233	38248	TAGAATAACACCCCCT	68	V	2440
1485629	43535	43550	45601	45616	TAAATCTTGTTCACTG	29	V	2441
1485654	35242	35257	37308	37323	ATTACAATAAAGTCC	39	V	2442
1485670	39894	39909	41960	41975	AAGATAAGACCTGTAA	26	V	2443
1485700	20952	20967	23018	23033	TAGAATTCATCTATCA	36	V	2444

1485714	33829	33844	35895	35910	GAATCATATGATACAC	21	V	2445
1485739	26373	26388	28439	28454	GTAATAGTTACTTAGT	24	V	2446
1485749	55232	55247	57298	57313	TAGGATTAAACAGTCC	20	V	2447
1485765	28106	28121	30172	30187	CAGGTTAACAAAAGTA	31	V	2448
1485775	49174	49189	51240	51255	TAGTACACATTCAGAA	66	V	2449
1485805	21602	21617	23668	23683	TATGATTTAAACCTAT	96	V	2450
1485831	46304	46319	48370	48385	TCCTAGCGATGGAGTA	52	V	2451
1485919	71487	71502	73553	73568	AGTTTAACTAAGAGTT	29	V	2452
1485921	39269	39284	41335	41350	CCCTATATCTCAACTC	35	V	2453
1485922	45597	45612	47663	47678	TCTATTAATACCTCCT	49	V	2454
1485927	41530	41545	43596	43611	TATATCACAAAGTACC	55	V	2455
1486098	72109	72124	74175	74190	TCGAGATTAGTTCTTC	31	V	2456
1486130	39761	39776	41827	41842	CACATTAACACTCAT	39	V	2457
1486137	40376	40391	42442	42457	GACTTTAAATCTATGC	19	V	2458
1486171	31217	31232	33283	33298	AAACGATTTCACTGGC	11	V	2459
1486260	29393	29408	31459	31474	AAGGGTTAGATATAAA	46	V	2460
1486262	84271	84286	86337	86352	GACTATCATGAACCAT	50	V	2461
1486307	14572	14587	16638	16653	CTATTCACATGACTAT	47	V	2462
1486315	27484	27499	29550	29565	CCATTATTCGTCTAAA	28	V	2463
1486345	25621	25636	27687	27702	TGGAATACGTCCGCGG	23	V	2464
1486354	87432	87447	89498	89513	GATATTCTTTAAACC	31	V	2465
1486365	37242	37257	39308	39323	GACTATTCTCGCCCTG	46	V	2466
1486378	21377	21392	23443	23458	TATCATGGCTACTATC	33	V	2467
1486457	86267	86282	88333	88348	ATAGTTTTTCATGCTAC	51	V	2468
1486473	86808	86823	88874	88889	GGACAATGTCTATCCA	74	V	2469
1486483	45337	45352	47403	47418	CCCTACTGAATTACCA	57	V	2470
1486572	74982	74997	77048	77063	TCTATTCAGACACCAA	32	V	2471
1486614	20629	20644	22695	22710	ATATACCTAATAGTCA	41	V	2472
1486615	25996	26011	28062	28077	GCAAACCACTGCATGG	19	V	2473
1486630	24977	24992	27043	27058	AGGGATATTCCTGTC	69	V	2474
1486686	16667	16682	18733	18748	AGTTATAATATCTTTG	25	V	2475
1482271	45359	45374	47425	47440	TCGTATTAGTTTTCTA	20	W	2476
1482416	89944	89959	92010	92025	GTTATACCACATTTCA	43	W	2477
1482563	14573	14588	16639	16654	GCTATTCACATGACTA	53	W	2478
1482633	33332	33347	35398	35413	GCAGATGTAAATTTTC	9	W	2479
1482635	39762	39777	41828	41843	ACACATTAACACTCA	32	W	2480
1483096	48864	48879	50930	50945	GTAAAGGTTTTTCATCA	33	W	2481
1483134	23227	23242	25293	25308	GTATGTACAACCTCAG	15	W	2482
1483208	2641	2656	4707	4722	ACATCCATGGCTAATG	38	W	2483
1483363	36707	36722	38773	38788	CCTTTATTATTCTCAG	28	W	2484
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	20	W	19
1483968	15511	15526	17577	17592	AAGTTAATTTCCACCA	66	W	2485
1484352	18572	18587	20638	20653	AAGGTTATCCAGTCAG	6	W	2486

1484487	39895	39910	41961	41976	AAAGATAAGACCTGTA	73	W	2487
1484524	24260	24275	26326	26341	CTAATTATACCATGTG	20	W	2488
1484560	21380	21395	23446	23461	AAATATCATGGCTACT	86	W	2489
1484643	27486	27501	29552	29567	ATCCATTATTCGTCTA	30	W	2490
1484671	26376	26391	28442	28457	CCAGTAATAGTTACTT	16	W	2491
1484702	37770	37785	39836	39851	GCTAAATATTACTCAC	38	W	2492
1484802	75496	75511	77562	77577	GAGGTAATACAATCCA	40	W	2493
1484823	19547	19562	21613	21628	AAGCAGATCTTTC TTC	49	W	2494
1484834	22751	22766	24817	24832	TTAAATGCTACTTTGG	21	W	2495
1484943	46309	46324	48375	48390	TATGATCCTAGCGATG	65	W	2496
1484973	86868	86883	88934	88949	AACCTATTACAGGCAT	47	W	2497
1485046	19073	19088	21139	21154	GATACCCTCAAAGGGC	67	W	2498
1485085	34313	34328	36379	36394	AGAAATTGTCAACCTA	47	W	2499
1485090	38016	38031	40082	40097	AAGTTTACTATCTTAC	76	W	2500
1485132	20630	20645	22696	22711	AATATACCTAATAGTC	65	W	2501
1485159	100156	100171	102222	102237	TTGGATAGACTCGGTT	43	W	2502
1485160	35247	35262	37313	37328	ACCTTATTACA ACTAA	29	W	2503
1485173	16072	16087	18138	18153	AACGTACACAGCCATA	75	W	2504
1485175	49175	49190	51241	51256	ATAGTACACATTCAGA	33	W	2505
1485178	20103	20118	22169	22184	ACAGAATATACACGTG	24	W	2506
1485205	30094	30109	32160	32175	TCATGATAAGTATACA	45	W	2507
1485240	39272	39287	41338	41353	TACCCCTATATCTCAA	63	W	2508
1485248	27247	27262	29313	29328	TACTATGATACTTCAC	41	W	2509
1485283	84307	84322	86373	86388	AGTACAACATCTGTTT	70	W	2510
1485287	33838	33853	35904	35919	TATAGACAAGAATCAT	56	W	2511
1485381	87470	87485	89536	89551	GAATTTCTTTGACTGT	33	W	2512
1485428	25997	26012	28063	28078	AGCAAACCACTGCATG	49	W	2513
1485447	22315	22330	24381	24396	GGCAGAAAAGTCAAGT	31	W	2514
1485513	28121	28136	30187	30202	CTATATATCGTCAGAC	24	W	2515
1485533	48631	48646	50697	50712	CTTTTAGCTCCTAGGG	85	W	2516
1485576	71028	71043	73094	73109	ATCATACTCAGATATT	49	W	2517
1485580	36168	36183	38234	38249	TTAGAATAACACCCCC	66	W	2518
1485627	37247	37262	39313	39328	ATATTGACTATTCTCG	46	W	2519
1485645	72121	72136	74187	74202	CCAAAAATATGCTCGA	41	W	2520
1485658	30712	30727	32778	32793	ACACTATATTCCTCAG	35	W	2521
1485691	86287	86302	88353	88368	GATCTAAGGACCCTCA	101	W	2522
1485692	46797	46812	48863	48878	ATATTGACTCCTCCAA	60	W	2523
1485754	17437	17452	19503	19518	TTCAAGATATTCATCC	29	W	2524
1485760	31218	31233	33284	33299	CAAACGATTTCACTGG	35	W	2525
1485762	43536	43551	45602	45617	GTAAATCTTGTTCACT	29	W	2526
1485813	47940	47955	50006	50021	ACTCTACATATTTAGG	37	W	2527
1485893	55366	55381	57432	57447	AGCATTAATCTACAGA	15	W	2528
1485916	42563	42578	44629	44644	GGCATAATAAGTCATA	13	W	2529

1486030	20957	20972	23023	23038	GTCATTAGAATTCAC	23	W	2530
1486077	32599	32614	34665	34680	TTCTATCCTAGAATTC	61	W	2531
1486078	43915	43930	45981	45996	TAATGTACTTTTCCTC	42	W	2532
1486079	38755	38770	40821	40836	CGACAAATTCAGCTT	47	W	2533
1486099	32993	33008	35059	35074	TGTTAGACATTCAC	57	W	2534
1486202	23631	23646	25697	25712	TGCAGTTAAACCACGA	35	W	2535
1486203	70269	70284	72335	72350	CAGCTTAATATCCTCC	48	W	2536
1486289	40919	40934	42985	43000	GATATCACAACATACAT	42	W	2537
1486290	71580	71595	73646	73661	CTCTTTAACAGTATGT	34	W	2538
1486335	44925	44940	46991	47006	TCTTAAGTCTCATATG	47	W	2539
1486336	28849	28864	30915	30930	CTGAAACAACACTACC	75	W	2540
1486350	29471	29486	31537	31552	GTGGTAACAGTAGAGA	67	W	2541
1486356	31983	31998	34049	34064	TATATCATACTAACTT	79	W	2542
1486369	44339	44354	46405	46420	CATCCCTACATACTCA	69	W	2543
1486385	25622	25637	27688	27703	GTGGAATACGTCCGCG	60	W	2544
1486402	24978	24993	27044	27059	TAGGGATATTCCCGTC	78	W	2545
1486447	106465	106480	108531	108546	TCCAATAACTTCATCA	82	W	2546
1486577	18079	18094	20145	20160	TCTATTCCAAATGACT	50	W	2547
1486628	41536	41551	43602	43617	TACCTATATATCACAA	84	W	2548
1486632	21646	21661	23712	23727	AAGCTATGTTAAACAT	32	W	2549
1486634	45598	45613	47664	47679	CTCTATTAATACCTCC	27	W	2550
1486640	40377	40392	42443	42458	TGACTTTAAATCTATG	69	W	2551
1486682	16670	16685	18736	18751	GAAAGTTATAATATCT	35	W	2552
1482152	32618	32633	34684	34699	GAACATTTCTCACTCA	41	X	2553
1482215	40449	40464	42515	42530	TAGAACTTACAGATGA	20	X	2554
1482286	42565	42580	44631	44646	TAGGCATAATAAGTCA	48	X	2555
1482590	49176	49191	51242	51257	TATAGTACACATTCAG	44	X	2556
1482736	2642	2657	4708	4723	TACATCCATGGCTAAT	25	X	2557
1482920	18573	18588	20639	20654	AAAGGTTATCCAGTCA	15	X	2558
1483203	30713	30728	32779	32794	GACACTATATTCCTCA	29	X	2559
1483434	48865	48880	50931	50946	GGTAAAGGTTTTTCATC	45	X	2560
1483608	46798	46813	48864	48879	GATATTGACTCCTCCA	20	X	2561
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	21	X	19
1484220	22808	22823	24874	24889	GCATAATTTCTGGCTC	14	X	2562
1484489	75520	75535	77586	77601	GAGAATTCCATTCTGC	41	X	2563
1484499	16692	16707	18758	18773	GTATTAGTTCCATATT	28	X	2564
1484536	28122	28137	30188	30203	CCTATATATCGTCAGA	48	X	2565
1484561	29486	29501	31552	31567	AAGGCCTAGCCTAGGG	72	X	2566
1484568	34315	34330	36381	36396	TAAGAAATTGTCAACC	69	X	2567
1484588	16076	16091	18142	18157	ACAAAACGTACACAGC	63	X	2568
1484624	39950	39965	42016	42031	GAGTTAAGCATTTCAGA	12	X	2569
1484633	44927	44942	46993	47008	CATCTTAAGTCTCATA	50	X	2570
1484645	20958	20973	23024	23039	GGTCATTAGAATTCAC	15	X	2571

1484669	48644	48659	50710	50725	ACATTAAATACGTCTT	55	X	2572
1484738	25651	25666	27717	27732	ACATCTTAGTAGAAGA	40	X	2573
1484748	30099	30114	32165	32180	AGCTATCATGATAAGT	36	X	2574
1484756	31219	31234	33285	33300	TCAAACGATTTCACTG	56	X	2575
1484770	41537	41552	43603	43618	CTACCTATATATCACA	70	X	2576
1484800	27488	27503	29554	29569	CAATCCATTATTCGTC	37	X	2577
1484805	24999	25014	27065	27080	GAAACCAGACTCTCTG	53	X	2578
1484810	26052	26067	28118	28133	AATAGCATCCTTCCAC	57	X	2579
1484816	36169	36184	38235	38250	ATTAGAATAACACCCC	62	X	2580
1484829	106767	106782	108833	108848	ACGTATATATAGCTCA	19	X	2581
1484832	71586	71601	73652	73667	CGCAATCTCTTTAACA	53	X	2582
1484883	31987	32002	34053	34068	ACATTATATCATACTA	59	X	2583
1484887	33843	33858	35909	35924	GAATATATAGACAAGA	29	X	2584
1484909	22336	22351	24402	24417	CTAACAGCCTATGCTT	58	X	2585
1484964	55832	55847	57898	57913	CTAATACTAACTTCCA	56	X	2586
1484982	32995	33010	35061	35076	AATGTTAGACATTAC	40	X	2587
1485029	72122	72137	74188	74203	TCCAAAAATATGCTCG	45	X	2588
1485054	70282	70297	72348	72363	GACTTATTTCCACAG	38	X	2589
1485077	90862	90877	92928	92943	GTTATATTTACACTGC	15	X	2590
1485106	87490	87505	89556	89571	CTATTAGTCAATTCTC	47	X	2591
1485128	27248	27263	29314	29329	GTACTATGATACTTCA	22	X	2592
1485143	45360	45375	47426	47441	ATCGTATTAGTTTTCT	26	X	2593
1485166	19558	19573	21624	21639	ATTCTTAGAACAAGCA	12	X	2594
1485206	26403	26418	28469	28484	GCAATAATCCAGACTG	10	X	2595
1485244	35248	35263	37314	37329	TACCTTATTACAATA	34	X	2596
1485249	21654	21669	23720	23735	AGAATTTTAAGCTATG	49	X	2597
1485317	28882	28897	30948	30963	GATGAATGAAGCTCTGG	31	X	2598
1485410	23652	23667	25718	25733	GTATATGACCAAACAA	58	X	2599
1485453	43540	43555	45606	45621	AAGGGTAAATCTTGTT	23	X	2600
1485483	43916	43931	45982	45997	GTAATGTACTTTTCCT	54	X	2601
1485520	14598	14613	16664	16679	AGTTACACCATGTCAG	90	X	2602
1485546	84903	84918	86969	86984	GCAGATTTGTTCTTCA	25	X	2603
1485565	19159	19174	21225	21240	GTTCAGAATTATGTCA	20	X	2604
1485757	71031	71046	73097	73112	CAAATCATACTCAGAT	39	X	2605
1485794	38017	38032	40083	40098	CAAGTTTACTATCTTA	77	X	2606
1485853	101148	101163	103214	103229	ATTACTATGTCATCAG	54	X	2607
1485854	86288	86303	88354	88369	GGATCTAAGGACCCTC	88	X	2608
1485862	86869	86884	88935	88950	TAACCTATTACAGGCA	52	X	2609
1485913	39764	39779	41830	41845	GTACACATTAACACT	64	X	2610
1485926	20104	20119	22170	22185	TACAGAATATACACGT	25	X	2611
1485942	23247	23262	25313	25328	TGGAACCTCAAGGCAA	20	X	2612
1485949	20635	20650	22701	22716	GTCTAAATATACCTAA	51	X	2613
1485971	40922	40937	42988	43003	AGTGATATCACAACTA	78	X	2614

1485994	37784	37799	39850	39865	GACAAACCTGGCTTGC	51	X	2615
1486043	17484	17499	19550	19565	ACAACCCAGAATAGTT	49	X	2616
1486100	24261	24276	26327	26342	TCTAATTATACCATGT	36	X	2617
1486183	46040	46055	48106	48121	CTCTTAAAAGCCCACC	35	X	2618
1486301	47947	47962	50013	50028	GAATTGTACTCTACAT	18	X	2619
1486346	46312	46327	48378	48393	TGATATGATCCTAGCG	60	X	2620
1486355	15512	15527	17578	17593	CAAGTTAATTTCCACC	56	X	2621
1486361	37248	37263	39314	39329	GATATTGACTATTCTC	16	X	2622
1486395	21384	21399	23450	23465	GCTAAAATATCATGGC	73	X	2623
1486410	36771	36786	38837	38852	CATACTTTGATTTGCT	17	X	2624
1486431	44348	44363	46414	46429	GATACTGGACATCCCT	39	X	2625
1486488	33346	33361	35412	35427	CTCCATCACACCTTGC	36	X	2626
1486494	39274	39289	41340	41355	TTTACCCCTATATCTC	27	X	2627
1486529	38757	38772	40823	40838	AACGACAAATTCCAGC	44	X	2628
1486602	18102	18117	20168	20183	GGAAAAGTACTACTGG	11	X	2629
1482283	45415	45430	47481	47496	AGGTATTATTTGTCAC	5	Y	2630
1482385	15513	15528	17579	17594	GCAAGTTAATTTCCAC	39	Y	2631
1482665	28123	28138	30189	30204	TCCTATATATCGTCAG	25	Y	2632
1483020	48866	48881	50932	50947	AGGTAAAGGTTTTCAT	28	Y	2633
1483121	27490	27505	29556	29571	GACAATCCATTATTCG	16	Y	2634
1483302	18620	18635	20686	20701	TAGTAGAGCTTCCTCA	42	Y	2635
1483470	44928	44943	46994	47009	ACATCTTAAGTCTCAT	38	Y	2636
1483558	31232	31247	33298	33313	CAAGCCATCTAGCTCA	31	Y	2637
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	17	Y	19
1484246	2643	2658	4709	4724	ATACATCCATGGCTAA	23	Y	2638
1484533	87492	87507	89558	89573	ATCTATTAGTCAATTC	34	Y	2639
1484550	46041	46056	48107	48122	CCTCTTAAAAGCCCAC	29	Y	2640
1484605	40450	40465	42516	42531	GTAGAACTTACAGATG	26	Y	2641
1484616	71032	71047	73098	73113	TCAAATCATACTCAGA	16	Y	2642
1484618	38019	38034	40085	40100	GTCAAGTTTACTATCT	31	Y	2643
1484677	39278	39293	41344	41359	GTATTTTACCCCTATA	44	Y	2644
1484697	33446	33461	35512	35527	AAGCAATAAACTTCCT	41	Y	2645
1484722	42628	42643	44694	44709	ACAATACCTGCCTTCG	48	Y	2646
1484958	30140	30155	32206	32221	ATGTACAATAAGTAGT	36	Y	2647
1484978	35249	35264	37315	37330	ATACCTTATTACAACCT	53	Y	2648
1485017	48645	48660	50711	50726	TACATTAAATACGTCT	27	Y	2649
1485043	19226	19241	21292	21307	AGCTACATTCATATGA	34	Y	2650
1485145	107312	107327	109378	109393	TAGTGATCAAACGGGA	42	Y	2651
1485170	44349	44364	46415	46430	CGATACTGGACATCCC	44	Y	2652
1485208	34320	34335	36386	36401	CTTCGTAAGAAATTGT	26	Y	2653
1485251	21385	21400	23451	23466	AGCTAAAATATCATGG	12	Y	2654
1485339	71622	71637	73688	73703	ATACATTTTGCCTCTG	35	Y	2655
1485358	41539	41554	43605	43620	CTCTACCTATATATCA	73	Y	2656

1485385	16079	16094	18145	18160	AACACAAAACGTACAC	60	Y	2657
1485418	23653	23668	25719	25734	TGTATATGACCAAACA	49	Y	2658
1485427	47949	47964	50015	50030	ATGAATTGTACTCTAC	45	Y	2659
1485429	29587	29602	31653	31668	GAATTATTCCGACTGC	38	Y	2660
1485456	21655	21670	23721	23736	CAGAATTTTAAGCTAT	39	Y	2661
1485461	86312	86327	88378	88393	ACCTACTTTCACAGCA	79	Y	2662
1485534	36197	36212	38263	38278	AAATGTCTCACAATGC	25	Y	2663
1485561	76633	76648	78699	78714	GACTATAAACCTTTCA	56	Y	2664
1485602	24265	24280	26331	26346	CCATTCTAATTATACC	22	Y	2665
1485611	30716	30731	32782	32797	AATGACACTATATTCC	48	Y	2666
1485632	43919	43934	45985	46000	CCTGTAATGTACTTTT	50	Y	2667
1485650	85417	85432	87483	87498	ACCCTTAAAGCCTTCA	43	Y	2668
1485677	22337	22352	24403	24418	GCTAACAGCCTATGCT	71	Y	2669
1485682	14602	14617	16668	16683	GAGGAGTTACACCATG	87	Y	2670
1485690	72146	72161	74212	74227	AGCACAAACAATTTGG	30	Y	2671
1485701	25706	25721	27772	27787	GAAACATCAGCTGAGG	8	Y	2672
1485738	40958	40973	43024	43039	TCCTACCCAATTCTCC	62	Y	2673
1485770	23269	23284	25335	25350	ACTCAATCCACTGAGC	47	Y	2674
1485786	39766	39781	41832	41847	TAGTACACATTA ACTA	73	Y	2675
1485835	101617	101632	103683	103698	CTATTTCAATGTAGCA	29	Y	2676
1485846	38759	38774	40825	40840	CAAACGACAAATTCCA	49	Y	2677
1485884	33847	33862	35913	35928	GTATGAATATATAGAC	23	Y	2678
1485956	31988	32003	34054	34069	GACATTATATCATACT	32	Y	2679
1485963	20636	20651	22702	22717	GGTCTAAATATACCTA	45	Y	2680
1486019	43564	43579	45630	45645	AAGTAGCCGCTACTGC	69	Y	2681
1486044	20159	20174	22225	22240	ATTCATCTAGCACACA	31	Y	2682
1486051	70315	70330	72381	72396	AGATTATGCAATTTTG	11	Y	2683
1486082	55833	55848	57899	57914	TCTAATACTAACTTCC	55	Y	2684
1486142	27249	27264	29315	29330	TGTACTATGATACTTC	22	Y	2685
1486157	19559	19574	21625	21640	TATTC'TTAGAACAAGC	21	Y	2686
1486217	36772	36787	38838	38853	TCATACTTTGATTTGC	13	Y	2687
1486233	20996	21011	23062	23077	ACAGAGTACTTTCCCA	47	Y	2688
1486240	40058	40073	42124	42139	AATACCACATACTCAT	41	Y	2689
1486270	37792	37807	39858	39873	TCTCTAAAGACAAACC	49	Y	2690
1486273	28960	28975	31026	31041	ACACTATATTAAAGGA	26	Y	2691
1486352	26404	26419	28470	28485	CGCAATAATCCAGACT	22	Y	2692
1486358	18164	18179	20230	20245	TGTATAAAGACCCAAA	26	Y	2693
1486363	25005	25020	27071	27086	CAGGATGAAACCAGAC	23	Y	2694
1486368	32996	33011	35062	35077	CAATGTTAGACATTCA	18	Y	2695
1486425	37249	37264	39315	39330	AGATATTGACTATTCT	61	Y	2696
1486437	16693	16708	18759	18774	TGTATTAGTTCCATAT	25	Y	2697
1486477	26054	26069	28120	28135	ACAATAGCATCCTTCC	47	Y	2698
1486543	32623	32638	34689	34704	CCTAAGAACATTTCTC	49	Y	2699

1486561	17504	17519	19570	19585	TAGGATTACATGAAGT	22	Y	2700
1486580	49177	49192	51243	51258	GTATAGTACACATTCA	19	Y	2701
1486604	46799	46814	48865	48880	GGATATTGACTCCTCC	49	Y	2702
1486652	22811	22826	24877	24892	CAAGCATAATTTCTGG	19	Y	2703
1486656	46313	46328	48379	48394	CTGATATGATCCTAGC	53	Y	2704
1486676	86870	86885	88936	88951	TTAACCTATTACAGGC	41	Y	2705
1486681	91800	91815	93866	93881	ATTATTTGACTATCAG	40	Y	2706
1482394	45416	45431	47482	47497	TAGGTATTATTTGTCA	13	Z	2707
1483093	34330	34345	36396	36411	TATAGTTTAGCTTCGT	33	Z	2708
1483322	48867	48882	50933	50948	AAGGTAAAGGTTTTCA	36	Z	2709
1483724	47950	47965	50016	50031	AATGAATTGTACTCTA	54	Z	2710
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	17	Z	19
1484061	20162	20177	22228	22243	TTTATTCATCTAGCAC	25	Z	2711
1484151	2644	2659	4710	4725	AATACATCCATGGCTA	28	Z	2712
1484508	70382	70397	72448	72463	CCGGTAACCACTGTTT	43	Z	2713
1484521	85419	85434	87485	87500	ACACCCTTAAAGCCTT	46	Z	2714
1484549	23272	23287	25338	25353	TATACTCAATCCACTG	32	Z	2715
1484581	31989	32004	34055	34070	AGACATTATATCATAAC	48	Z	2716
1484582	101618	101633	103684	103699	ACTATTTCAATGTAGC	39	Z	2717
1484594	46062	46077	48128	48143	ACAAACCTTAGCTTGC	22	Z	2718
1484596	38043	38058	40109	40124	GCAAACATGTATAGCT	53	Z	2719
1484631	43972	43987	46038	46053	GTAATAATATTCGCTA	25	Z	2720
1484651	26405	26420	28471	28486	ACGCAATAATCCAGAC	29	Z	2721
1484690	28984	28999	31050	31065	GCTAGAAATTTCCAGA	54	Z	2722
1484723	19266	19281	21332	21347	CCTTTAACTAGTCTTA	16	Z	2723
1484740	71649	71664	73715	73730	CTAAACGGTGCAGGAC	40	Z	2724
1484835	87495	87510	89561	89576	TATATCTATTAGTCAA	52	Z	2725
1484872	32626	32641	34692	34707	AGGCCTAAGAACATTT	88	Z	2726
1484905	72152	72167	74218	74233	TTGCTAAGCACAAACA	38	Z	2727
1484916	21724	21739	23790	23805	AGACGTTAGCACATGC	24	Z	2728
1484924	16081	16096	18147	18162	GTAACACAAAACGTAC	69	Z	2729
1484985	42833	42848	44899	44914	GCTACCAGACTAGCTG	93	Z	2730
1485002	27495	27510	29561	29576	GGCAAGACAATCCATT	35	Z	2731
1485059	43568	43583	45634	45649	CATAAAGTAGCCGCTA	77	Z	2732
1485067	22362	22377	24428	24443	ATCAATGTCTCCCTAA	40	Z	2733
1485078	14618	14633	16684	16699	ATAAGCCTCAGTCTGA	79	Z	2734
1485107	37813	37828	39879	39894	TGTATAAACCCACAA	84	Z	2735
1485124	44937	44952	47003	47018	TATACTCAGACATCTT	20	Z	2736
1485129	31245	31260	33311	33326	AAGCTATGACCCTCAA	34	Z	2737
1485136	30141	30156	32207	32222	CATGTACAATAAGTAG	14	Z	2738
1485154	91988	92003	94054	94069	CATAATTCAAGTCAGG	24	Z	2739
1485162	20638	20653	22704	22719	TAGGTCTAAATATACC	30	Z	2740
1485176	22846	22861	24912	24927	CACTTACTTGTTCAAT	36	Z	2741

1485228	19565	19580	21631	21646	GTACAATATTCTTAGA	38	Z	2742
1485309	18165	18180	20231	20246	ATGTATAAAGACCCAA	29	Z	2743
1485314	18627	18642	20693	20708	AATTTTCTAGTAGAGC	39	Z	2744
1485318	24274	24289	26340	26355	GCAGAGAATCCATTCT	26	Z	2745
1485404	21386	21401	23452	23467	CAGCTAAAATATCATG	40	Z	2746
1485433	16694	16709	18760	18775	CTGTATTAGTTCCATA	12	Z	2747
1485458	15515	15530	17581	17596	CAGCAAGTTAATTTCC	66	Z	2748
1485482	26055	26070	28121	28136	AACAATAGCATCCTTC	41	Z	2749
1485494	40452	40467	42518	42533	GGGTAGAACTTACAGA	19	Z	2750
1485508	39770	39785	41836	41851	CTTATAGTACACATTA	25	Z	2751
1485519	17554	17569	19620	19635	GCCTTTTTATTATCAG	21	Z	2752
1485522	38760	38775	40826	40841	TCAAACGACAAATTCC	46	Z	2753
1485567	36796	36811	38862	38877	TAATCACTGACACCTA	52	Z	2754
1485582	46801	46816	48867	48882	ATGGATATTGACTCCT	46	Z	2755
1485648	44389	44404	46455	46470	CAGCCCTATAAGAACC	39	Z	2756
1485678	76972	76987	79038	79053	TATCTTCAATCATTGT	51	Z	2757
1485696	25708	25723	27774	27789	ATGAAACATCAGCTGA	36	Z	2758
1485716	25049	25064	27115	27130	TTGTAGATTCACCCCA	24	Z	2759
1485761	71033	71048	73099	73114	ATCAAATCATACTCAG	20	Z	2760
1485810	86874	86889	88940	88955	GCATTTAACCTATTAC	42	Z	2761
1485828	28149	28164	30215	30230	GTATCAAAAACCTGCAC	27	Z	2762
1485842	29589	29604	31655	31670	AAGAATTATTCCGACT	53	Z	2763
1485868	33458	33473	35524	35539	GCACAATTTGATAAGC	23	Z	2764
1485875	23654	23669	25720	25735	CTGTATATGACCAAAC	54	Z	2765
1485903	107455	107470	109521	109536	GTAGATACGCCTCTGC	67	Z	2766
1485924	37250	37265	39316	39331	CAGATATTGACTATTTC	32	Z	2767
1485950	41555	41570	43621	43636	CACAAGACTTCATCTT	37	Z	2768
1485954	33865	33880	35931	35946	GAACACTTTTTCTGAT	25	Z	2769
1485964	39304	39319	41370	41385	TCATAATATGTCTTGA	66	Z	2770
1486045	48665	48680	50731	50746	CTTATTTCCACCACAC	21	Z	2771
1486063	49179	49194	51245	51260	GTGTATAGTACACATT	43	Z	2772
1486073	40987	41002	43053	43068	CTTGTAAGTGCCTGT	34	Z	2773
1486136	35250	35265	37316	37331	GATACCTTATTACAAC	27	Z	2774
1486168	30842	30857	32908	32923	TAATTCGTTTTTCACA	61	Z	2775
1486333	27250	27265	29316	29331	ATGTACTATGATACTT	34	Z	2776
1486342	86313	86328	88379	88394	TACCTACTTTCACAGC	70	Z	2777
1486504	46314	46329	48380	48395	CCTGATATGATCCTAG	55	Z	2778
1486533	33000	33015	35066	35081	GAATCAATGTTAGACA	24	Z	2779
1486571	56418	56433	58484	58499	TCTTTTATGTACATGG	23	Z	2780
1486624	40059	40074	42125	42140	GAATACCACATACTCA	40	Z	2781
1486642	36202	36217	38268	38283	GCAGAAAATGTCTCAC	16	Z	2782
1486692	21032	21047	23098	23113	AGTAAGCCTATTTTCC	23	Z	2783
1482234	40478	40493	42544	42559	TCCATTAATCTTAAGT	27	AA	2784

1482373	48868	48883	50934	50949	GAAGGTAAAGGTTTTTC	33	AA	2785
1482860	2645	2660	4711	4726	GAATACATCCATGGCT	34	AA	2786
1482916	19587	19602	21653	21668	GCTGATTCAAGTCACT	11	AA	2787
1483423	44506	44521	46572	46587	AAGGATTCACTTTCAG	13	AA	2788
1483635	16695	16710	18761	18776	ACTGTATTAGTTCCAT	6	AA	2789
1483716	18166	18181	20232	20247	AATGTATAAAGACCCA	20	AA	2790
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	13	AA	19
1484293	22374	22389	24440	24455	GCAAATAGCATCATCA	28	AA	2791
1484296	26057	26072	28123	28138	GCAACAATAGCATCCT	12	AA	2792
1484482	37814	37829	39880	39895	TTGTATAAACCCACACA	62	AA	2793
1484546	20670	20685	22736	22751	AGGCAATTCATTGTGT	14	AA	2794
1484563	25731	25746	27797	27812	TCTAACATAAAGTTGC	41	AA	2795
1484574	39305	39320	41371	41386	TTCATAATATGTCTTG	21	AA	2796
1484576	39771	39786	41837	41852	GCTTATAGTACACATT	17	AA	2797
1484607	43973	43988	46039	46054	AGTAATAATATTCGCT	23	AA	2798
1484639	36797	36812	38863	38878	ATAATCACTGACACCT	44	AA	2799
1484652	16104	16119	18170	18185	CGTAATCTCACCAGCT	18	AA	2800
1484660	22953	22968	25019	25034	CCAATTAGATTTATCA	16	AA	2801
1484766	43616	43631	45682	45697	GACTACTTGATGTCTA	54	AA	2802
1484774	35336	35351	37402	37417	TATACTCCATTACCCCT	42	AA	2803
1484914	27251	27266	29317	29332	TATGTACTATGATACT	27	AA	2804
1484920	17594	17609	19660	19675	CATGTAGTAAATCTAA	67	AA	2805
1485016	49180	49195	51246	51261	AGTGTATAGTACACAT	77	AA	2806
1485032	21734	21749	23800	23815	TACTAACAATAGACGT	33	AA	2807
1485073	14622	14637	16688	16703	CCAGATAAGCCTCAGT	67	AA	2808
1485075	26406	26421	28472	28487	AACGCAATAATCCAGA	26	AA	2809
1485098	30142	30157	32208	32223	CCATGTACAATAAGTA	14	AA	2810
1485151	28151	28166	30217	30232	GTGTATCAAAAAGTGC	18	AA	2811
1485177	46813	46828	48879	48894	CTACCTTTAAAGATGG	24	AA	2812
1485209	48666	48681	50732	50747	ACTTATTTCCACCACA	34	AA	2813
1485237	29680	29695	31746	31761	CACAGTAAAGATTTGC	15	AA	2814
1485250	33470	33485	35536	35551	CAACTAACCACGGCAC	36	AA	2815
1485281	19267	19282	21333	21348	TCCTTTAACTAGTCTT	14	AA	2816
1485327	71062	71077	73128	73143	TATTATAATTCACCTCT	64	AA	2817
1485351	25059	25074	27125	27140	ATGTATCATATTGTAG	12	AA	2818
1485382	101620	101635	103686	103701	GCACTATTTCAATGTA	21	AA	2819
1485420	77770	77785	79836	79851	GTTTTAATATCTGTGC	34	AA	2820
1485464	38768	38783	40834	40849	AATATCAGTCAAACGA	33	AA	2821
1485470	70746	70761	72812	72827	TTAGATCTACATCTCC	49	AA	2822
1485524	28985	29000	31051	31066	GGCTAGAAATTTCCAG	42	AA	2823
1485685	40060	40075	42126	42141	TGAATACCACATACTC	14	AA	2824
1485751	27520	27535	29586	29601	ACAATAAATCACTCA	38	AA	2825
1485782	21034	21049	23100	23115	GCAGTAAGCCTATTTT	17	AA	2826

1485836	87496	87511	89562	89577	TTATATCTATTAGTCA	46	AA	2827
1485841	31246	31261	33312	33327	AAAGCTATGACCCTCA	45	AA	2828
1485881	33868	33883	35934	35949	GTAGAACACTTTTTCT	33	AA	2829
1485905	21387	21402	23453	23468	GCAGCTAAAATATCAT	25	AA	2830
1485931	71656	71671	73722	73737	TTTATTTCTAAACGGT	25	AA	2831
1485945	56832	56847	58898	58913	CCGTCTAGGTACTGCT	17	AA	2832
1485960	91990	92005	94056	94071	GCCATAATTCAAGTCA	34	AA	2833
1485980	36265	36280	38331	38346	GGACTATATAATAGGC	12	AA	2834
1486002	38044	38059	40110	40125	TGCAAACATGTATAGC	26	AA	2835
1486060	23745	23760	25811	25826	GATGACATCATCCAGT	22	AA	2836
1486226	86875	86890	88941	88956	AGCATTTAACCCTATTA	30	AA	2837
1486230	30884	30899	32950	32965	CTTGATCAATATTCAG	13	AA	2838
1486264	46063	46078	48129	48144	AACAAACCTTAGCTTG	58	AA	2839
1486266	40999	41014	43065	43080	AGCCAAGACTTTCTTG	41	AA	2840
1486268	23273	23288	25339	25354	ATATACTCAATCCACT	62	AA	2841
1486296	32627	32642	34693	34708	AAGGCCTAAGAACATT	49	AA	2842
1486347	32001	32016	34067	34082	AATATCAGCCAAAGAC	50	AA	2843
1486400	72184	72199	74250	74265	GAATCATTCTGAAGGG	25	AA	2844
1486417	42874	42889	44940	44955	GCAACCTCAACCATCC	64	AA	2845
1486430	46370	46385	48436	48451	TAATCCATAAGCTAGG	64	AA	2846
1486434	24364	24379	26430	26445	CATACAATATTAAGGC	11	AA	2847
1486449	47951	47966	50017	50032	GAATGAATTGTACTCT	18	AA	2848
1486491	20194	20209	22260	22275	GTCAAACCTGACATTT	26	AA	2849
1486505	85473	85488	87539	87554	ATCATATTCTAGCTAA	62	AA	2850
1486539	37251	37266	39317	39332	CCAGATATTGACTATT	20	AA	2851
1486549	86316	86331	88382	88397	TTGTACCTACTTTCAC	86	AA	2852
1486591	18628	18643	20694	20709	CAATTTTCTAGTAGAG	13	AA	2853
1486597	44938	44953	47004	47019	ATATACTCAGACATCT	31	AA	2854
1486609	41563	41578	43629	43644	TTAAATGTCACAAGAC	29	AA	2855
1486622	34334	34349	36400	36415	TAAGTATAGTTTAGCT	12	AA	2856
1486646	107762	107777	109828	109843	CAACGCGGCTGATTTT	72	AA	2857
1486671	45428	45443	47494	47509	ACAACATTTTTGTAGG	34	AA	2858
1486702	15531	15546	17597	17612	ATCCTTTGATCTCACT	64	AA	2859
1486706	33004	33019	35070	35085	TCAAGAATCAATGTTA	40	AA	2860
1482337	39363	39378	41429	41444	TGTTATAGTTTCTACA	58	AB	2861
1482437	20261	20276	22327	22342	CCAACATGACAGCCAT	24	AB	2862
1482595	33869	33884	35935	35950	AGTAGAACACTTTTTTC	16	AB	2863
1483004	48869	48884	50935	50950	GGAAGGTAAAGGTTTT	26	AB	2864
1483269	47983	47998	50049	50064	CCATTTTATAGCATGC	26	AB	2865
1483717	30148	30163	32214	32229	ACGTATCCATGTACAA	9	AB	2866
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	8	AB	19
1484031	87564	87579	89630	89645	TCATTTATGCTCAGTA	23	AB	2867
1484185	40487	40502	42553	42568	ACATATGCTTCCATTA	36	AB	2868

1484195	19279	19294	21345	21360	ATAACTCATTTGTCCT	16	AB	2869
1484229	23813	23828	25879	25894	GCATTTTGAACCTATT	10	AB	2870
1484311	2646	2661	4712	4727	TGAATACATCCATGGC	25	AB	2871
1484480	36798	36813	38864	38879	AATAATCACTGACACC	47	AB	2872
1484512	25060	25075	27126	27141	GATGTATCATATTGTA	8	AB	2873
1484567	44941	44956	47007	47022	GGAATATACTCAGACA	31	AB	2874
1484570	32005	32020	34071	34086	AGTTAATATCAGCCAA	26	AB	2875
1484597	44939	44954	47005	47020	AATATACTCAGACATC	34	AB	2876
	78164	78179	80230	80245				
1484653	27594	27609	29660	29675	AATAGTAAGAATTTGC	40	AB	2877
1484661	40061	40076	42127	42142	TTGAATACCACATACT	26	AB	2878
1484667	46372	46387	48438	48453	CCTAATCCATAAGCTA	59	AB	2879
1484713	92940	92955	95006	95021	GAAGCTTAGAACTTCA	87	AB	2880
1484791	29835	29850	31901	31916	TACATATTAATTGAGC	29	AB	2881
1484803	38812	38827	40878	40893	TACAACATTAGAACGA	30	AB	2882
1484845	17613	17628	19679	19694	GACACTAGACATGTAA	35	AB	2883
1484866	41564	41579	43630	43645	GTAAATGTCACAAGA	18	AB	2884
1484895	37252	37267	39318	39333	TCCAGATATTGACTAT	14	AB	2885
1484956	14623	14638	16689	16704	CCCAGATAAGCCTCAG	67	AB	2886
1485035	21398	21413	23464	23479	TCTATATCTAAGCAGC	31	AB	2887
1485045	35338	35353	37404	37419	CATATACTCCATTACC	59	AB	2888
1485127	16105	16120	18171	18186	CCGTAATCTCACCAGC	19	AB	2889
1485150	15576	15591	17642	17657	GAACCAGACTCAGCAT	62	AB	2890
1485161	33020	33035	35086	35101	AGAGAATTCCTGCTAC	46	AB	2891
1485172	39772	39787	41838	41853	TGCTTATAGTACACAT	27	AB	2892
1485202	22375	22390	24441	24456	AGCAAATAGCATCATC	23	AB	2893
1485214	34376	34391	36442	36457	GAACTTCTTTTAGCA	24	AB	2894
1485231	43975	43990	46041	46056	ATAGTAATAATATTCG	34	AB	2895
1485262	28176	28191	30242	30257	GTAGAAGTAAACGGGC	20	AB	2896
1485294	26059	26074	28125	28140	CTGCAACAATAGCATC	50	AB	2897
1485371	72188	72203	74254	74269	TCTAGAATCATTCTGA	51	AB	2898
1485372	37868	37883	39934	39949	ATAACCAGACTGACTG	45	AB	2899
1485384	71657	71672	73723	73738	TTTTATTTCTAAACGG	23	AB	2900
1485407	49216	49231	51282	51297	CAAAATATAGCTACAG	46	AB	2901
1485421	102185	102200	104251	104266	GTAAGTATATTCTGTC	32	AB	2902
1485443	25732	25747	27798	27813	CTCTAACATAAAGTTG	56	AB	2903
1485463	36310	36325	38376	38391	TGAAATCACCAAGGTC	43	AB	2904
1485501	48667	48682	50733	50748	AACTTATTTCCACCAC	37	AB	2905
1485542	85607	85622	87673	87688	GATAATGTTAATCTCC	24	AB	2906
1485562	26407	26422	28473	28488	GAACGCAATAATCCAG	20	AB	2907
1485577	24378	24393	26444	26459	AACTATTCCTCTTACA	61	AB	2908
1485657	57001	57016	59067	59082	CGATTAATCAACTGGC	11	AB	2909
1485666	44542	44557	46608	46623	CCACTATTATGATGGT	80	AB	2910

1485689	38234	38249	40300	40315	AATAGTCATAAGACTA	90	AB	2911
1485693	45439	45454	47505	47520	GCCTAGCATTTACAAC	53	AB	2912
1485725	27255	27270	29321	29336	ACTGTATGTACTATGA	19	AB	2913
1485796	108364	108379	110430	110445	ATCATTCAACTACTCA	41	AB	2914
1485818	33471	33486	35537	35552	ACAACCTAACCACGGCA	43	AB	2915
1485837	23274	23289	25340	25355	TATATACTCAATCCAC	47	AB	2916
1485855	21126	21141	23192	23207	CATATGTTACTCAGTT	34	AB	2917
1485886	41001	41016	43067	43082	GAAGCCAAGACTTTCT	53	AB	2918
1485928	46978	46993	49044	49059	ACCGTATCACTATGGA	34	AB	2919
1485962	86321	86336	88387	88402	AACAATTGTACCTACT	85	AB	2920
1485985	30892	30907	32958	32973	CTCTTAATCTTGATCA	28	AB	2921
1486071	18629	18644	20695	20710	ACAATTTTCTAGTAGA	16	AB	2922
1486205	19600	19615	21666	21681	ATTACAGAATAACGCT	32	AB	2923
1486257	46091	46106	48157	48172	TTTTTACACATGCAGT	32	AB	2924
1486285	21765	21780	23831	23846	AATTATCATGCCATCT	51	AB	2925
1486389	22954	22969	25020	25035	TCCAATTAGATTTATC	22	AB	2926
1486399	70748	70763	72814	72829	CCTTAGATCTACATCT	63	AB	2927
1486422	28987	29002	31053	31068	CTGGCTAGAAATTTCC	61	AB	2928
1486432	32660	32675	34726	34741	ACTATTACACAGAGAT	30	AB	2929
1486452	20682	20697	22748	22763	CAAATACAAATCAGGC	25	AB	2930
1486454	86876	86891	88942	88957	AAGCATTTAACCTATT	58	AB	2931
1486486	71140	71155	73206	73221	AAAGATCCTTCAGACA	49	AB	2932
1486542	31281	31296	33347	33362	ATCAATTATAAGAGGT	20	AB	2933
1486613	18167	18182	20233	20248	GAATGTATAAAGACCC	22	AB	2934
1486638	43652	43667	45718	45733	CTTACTTCTATTGCTA	42	AB	2935
1486657	16700	16715	18766	18781	CTCATACTGTATTAGT	18	AB	2936
1486664	42926	42941	44992	45007	GATCTTACTTTTTTGC	67	AB	2937
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	17	AC	19
1482345	2634	2649	4700	4715	TGGCTAATGAATTCCT	49	AD	2938
1482673	2664	2679	4730	4745	CCTTTGAAAGTCCTTT	22	AD	2939
1482708	20865	20880	22931	22946	CAGTTTATGTACCATT	11	AD	2940
1483091	44895	44910	46961	46976	TGATATCAACATGCCA	30	AD	2941
1483590	31102	31117	33168	33183	GATATCAATTGATTCC	21	AD	2942
1483729	48855	48870	50921	50936	TTCATCAATATCTGCA	22	AD	2943
1483842	48856	48871	50922	50937	TTTCATCAATATCTGC	13	AD	19
1483844	37718	37733	39784	39799	TCAGATATATTCCTGA	92	AD	2944
1483898	83529	83544	85595	85610	TCCATTTAGACTCCAA	31	AD	2945
1484492	39683	39698	41749	41764	AGAATTAATTGTCTTG	17	AD	2946
1484534	71306	71321	73372	73387	AATAGATATGACCTGT	61	AD	2947
1484557	23567	23582	25633	25648	CAGATATAGACCATCT	66	AD	2948
1484583	19425	19440	21491	21506	AAGGTATGAACTTCAA	8	AD	2949
1484584	72027	72042	74093	74108	ACTGAGATCCTATTTTC	96	AD	2950
1484586	27155	27170	29221	29236	TGATAGATAGACTCCT	56	AD	2951

1484681	47817	47832	49883	49898	GCATATCCTATGGAAA	22	AD	2952
1484691	19982	19997	22048	22063	ATAAATAACATCGCTG	35	AD	2953
1484716	46288	46303	48354	48369	CCTACCAACTTTCTTT	90	AD	2954
1484768	74624	74639	76690	76705	GATATTTCGATTCAAGA	61	AD	2955
1484771	41837	41852	43903	43918	ATCAGATCATAATCAA	29	AD	2956
1484782	24013	24028	26079	26094	AACTGTATAATGCACT	41	AD	2957
1484783	36546	36561	38612	38627	TCATACCTTATAAGTA	30	AD	2958
1484820	43409	43424	45475	45490	AGAAACTCCATATTGC	33	AD	2959
1484822	37989	38004	40055	40070	ACTATGCAAACTATAG	61	AD	2960
1484841	87347	87362	89413	89428	TTGTATAAAAACCATC	64	AD	2961
1484970	48538	48553	50604	50619	CTAATCAATAAAGCCT	72	AD	2962
1485015	45143	45158	47209	47224	ACGTTATACTTATTTT	21	AD	2963
1485034	86587	86602	88653	88668	TGACATACAAACCCAA	41	AD	2964
	87592	87607	89658	89673				
1485185	32868	32883	34934	34949	CAAGATAAATTTGCGA	74	AD	2965
1485238	38672	38687	40738	40753	GTAAAGTTAACCAGG	20	AD	2966
1485253	105149	105164	107215	107230	CTCATTTC AATAGTTA	37	AD	2967
1485286	25951	25966	28017	28032	TATGATCAAACTTCTA	53	AD	2968
1485336	98469	98484	100535	100550	ATATTACGCTGGGCTA	74	AD	2969
1485365	40812	40827	42878	42893	CTAACACCATCTTGGA	59	AD	2970
1485394	21514	21529	23580	23595	TCGCAATCAGTTCTTT	22	AD	2971
1485414	15492	15507	17558	17573	CTTCTAAGCAACACAA	82	AD	2972
1485510	86101	86116	88167	88182	TAAATTCAAGACTCCT	73	AD	2973
1485536	39861	39876	41927	41942	ATTACCGTCGTTAAAC	63	AD	2974
1485539	18438	18453	20504	20519	GAAACTATACTACCTA	61	AD	2975
1485548	25596	25611	27662	27677	CATGTATCAATTCTAA	56	AD	2976
1485556	41494	41509	43560	43575	GGTAATTAAGTTTTGG	36	AD	2977
1485597	17908	17923	19974	19989	TATAGCTTCTATTAGC	76	AD	2978
1485599	39184	39199	41250	41265	GTAGAGATCAACAGGA	29	AD	2979
1485607	30065	30080	32131	32146	TTTATTAGAATACCCT	28	AD	2980
1485646	32511	32526	34577	34592	TGTAAATAGAACCTAA	71	AD	2981
1485653	33156	33171	35222	35237	TAGAATTCAAGCCACA	43	AD	2982
1485655	16575	16590	18641	18656	AAAACATATCTCTGG	16	AD	2983
1485698	28005	28020	30071	30086	CTAGTATGGTCGAAAT	48	AD	2984
1485744	36095	36110	38161	38176	TGAAACATTAACCTGCT	47	AD	2985
1485785	27429	27444	29495	29510	CTGGATACCATACAAC	33	AD	2986
1485793	22173	22188	24239	24254	TCCAAGTTTATTATCA	27	AD	2987
1485821	22550	22565	24616	24631	TATCATCTAACTCTCA	38	AD	2988
1485877	43809	43824	45875	45890	TCCTTAACCTACAGAG	47	AD	2989
1485887	24721	24736	26787	26802	TGCAATCTACTTAGAC	61	AD	2990
1485937	70906	70921	72972	72987	GTCTATCTCACGTAGT	53	AD	2991
1485988	18980	18995	21046	21061	CAAGCTAGACATCCAG	16	AD	2992
1486005	33976	33991	36042	36057	ATGATACAAACCTTTC	49	AD	2993

1486087	17361	17376	19427	19442	TGATTATAAAAGACCC	23	AD	2994
1486219	37000	37015	39066	39081	GTCTAAACCTTCGTAA	68	AD	2995
1486232	44283	44298	46349	46364	TGAAGATGACCCATTG	62	AD	2996
1486242	20539	20554	22605	22620	ACAATTATTAGACACT	30	AD	2997
1486269	49075	49090	51141	51156	CCTGAATATTCACAAT	83	AD	2998
1486312	67606	67621	69672	69687	GTAGATATCATGTTCA	22	AD	2999
1486341	26253	26268	28319	28334	ATCCTACAATGAATGA	51	AD	3000
1486359	21248	21263	23314	23329	GATGGATATATACTTG	29	AD	3001
1486412	28518	28533	30584	30599	CTCCTAAAGCCTTCAT	48	AD	3002
1486414	30533	30548	32599	32614	TATATCAATAACCATG	41	AD	3003
1486470	46536	46551	48602	48617	ATCTCATACATTTAGA	46	AD	3004
1486471	40346	40361	42412	42427	CCGTATTGTTCTTCAT	24	AD	3005
1486511	29275	29290	31341	31356	AGGGATAACTTTTTGG	42	AD	3006
1486518	15862	15877	17928	17943	GACTTAAATCATTCC	74	AD	3007
1486545	45548	45563	47614	47629	ACGTACATCATTTGTT	31	AD	3008
1486593	53508	53523	55574	55589	AGACTATCAATCGGTA	35	AD	3009
1486601	31878	31893	33944	33959	TCAAACACATTCCCTA	53	AD	3010
1486606	88989	89004	91055	91070	GCCGTAGCTATAGTGC	61	AD	3011
1486653	35150	35165	37216	37231	GACAGTATCATAGAGA	20	AD	3012
1486666	33823	33838	35889	35904	TATGATACACCTGGAT	48	AD	3013
1486697	23189	23204	25255	25270	CCGTAACGTACACTGA	25	AD	3014

Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 3 (GENBANK Accession No: NM_001146055.1), as indicated. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

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Table 5

3-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 3 Start Site	SEQ ID NO: 3 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1482598	42	57	CTTTACACCACACTCT	35	C	3015
1482683	43	58	CCTTTACACCACACTC	45	F	3016

Example 2: Design and Effect of 3-10-4 cEt gapmers complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 17 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkddddd kkkk; wherein "k" represents a cEt sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified

oligonucleotides is (from 5' to 3'): soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 6

3-10-4 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535186	66281	66297	68347	68363	GTCAATATAGTCTCTGG	12	AN	3017
1535193	48858	48874	50924	50940	GGTTTTTCATCAATATCT	7	AN	3018
1535202	17435	17451	19501	19517	TCAAGATATTCATCCAA	10	AN	3019
1535203	26510	26526	28576	28592	AAGTTTAAACCAGTGCG	3	AN	3020
1535215	19424	19440	21490	21506	AAGGTATGAACCTCAAG	6	AN	3021
1535226	39949	39965	42015	42031	GAGTTAAGCATTCAGAT	6	AN	3022
1535237	20957	20973	23023	23039	GGTCATTAGAATTCCT	14	AN	3023
1535248	33039	33055	35105	35121	GCATAGAGATCCTCTCG	6	AN	3024
1535259	17128	17144	19194	19210	GGTGAATAACACTTTGG	10	AN	3025
1535270	45060	45076	47126	47142	GTTCAATACTATATCCA	5	AN	3026
1535281	19934	19950	22000	22016	GACATTCAAGCTTATT	3	AN	3027
1535292	19557	19573	21623	21639	ATTCTTAGAACAAGCAG	10	AN	3028
1535303	85916	85932	87982	87998	GCATTAACTCAATAGGT	10	AN	3029
1535314	19586	19602	21652	21668	GCTGATTCAAGTCACTT	9	AN	3030
1535315	18631	18647	20697	20713	TCAACAATTTTCTAGTA	9	AN	3031
1535327	48471	48487	50537	50553	TAGTTATTCTCAGCGGT	4	AN	3032
1535340	33023	33039	35089	35105	GCATAGAGAATTCCTGC	19	AN	3033
1535353	16105	16121	18171	18187	ACCGTAATCTCACCAGC	7	AN	3034
1535366	21224	21240	23290	23306	CCATATTGTTCTCAGAG	8	AN	3035
1535379	41387	41403	43453	43469	CTTACAATCATATGCAC	9	AN	3036
1535392	33869	33885	35935	35951	GAGTAGAACACTTTTTC	16	AN	3037

1535405	20820	20836	22886	22902	CAACTTTTACATACCAC	7	AN	3038
1535418	26737	26753	28803	28819	GTATTTTATACACAGCA	5	AN	3039
1535431	16665	16681	18731	18747	GTTATAATATCTTTGGT	5	AN	3040
1535439	18572	18588	20638	20654	AAAGGTTATCCAGTCAG	6	AN	3041
1535440	22511	22527	24577	24593	TGACAAATACAATTGGC	5	AN	3042
1535441	16195	16211	18261	18277	AAGGTAGCACTTTTCA	5	AN	3043
1535442	17726	17742	19792	19808	AGCATATTTTGTACAAA	10	AN	3044
1535443	32743	32759	34809	34825	GTCTAAAAATAGATCTGG	9	AN	3045
1535444	35939	35955	38005	38021	GTGAAATAAAGTTCCTA	5	AN	3046
1535445	34754	34770	36820	36836	GTGAATATCATGTAGCA	8	AN	3047
1535446	18735	18751	20801	20817	CCAGATTTTTTATGATC	3	AN	3048
1535447	26369	26385	28435	28451	ATAGTTACTTAGTTGCA	12	AN	3049
1535448	30208	30224	32274	32290	AGATTTATCTCATGAGT	3	AN	3050
1535449	31420	31436	33486	33502	GGTATTAATTTCAAGCT	6	AN	3051
1535450	45126	45142	47192	47208	CTGATTATATTTGCCT	21	AN	3052
1535451	22619	22635	24685	24701	ATTACTTCATATACGAG	6	AN	3053
1535452	22012	22028	24078	24094	AAAGTAGATTTTAGGCA	10	AN	3054
1535453	27931	27947	29997	30013	GGTAATAAAGTCACGGG	25	AN	3055
1535454	41666	41682	43732	43748	GCAAATATTGTAACCCC	30	AN	3056
1535455	18627	18643	20693	20709	CAATTTTCTAGTAGAGC	9	AN	3057
1535456	32177	32193	34243	34259	GCATTTCTAGCTTAGGT	4	AN	3058
1535462	27489	27505	29555	29571	GACAATCCATTATTCGT	16	AN	3059
1535473	45415	45431	47481	47497	TAGGTATTATTTGTCAC	3	AN	3060
1535474	23226	23242	25292	25308	GTATGTACAACCTCAGA	4	AN	3061
1535485	44505	44521	46571	46587	AAGGATTCACTTTCAGA	5	AN	3062
1535496	16694	16710	18760	18776	ACTGTATTAGTTCATA	5	AO	3063
1535507	21409	21425	23475	23491	GAAGTATTTGTCTCTAT	11	AO	3064
1535521	29226	29242	31292	31308	TGGATAAAATTCAGACA	4	AO	3065
1535542	33497	33513	35563	35579	GAGTTTACAATTTGGCA	6	AO	3066
1535563	21483	21499	23549	23565	GATGTATAGTCATGCAT	12	AO	3067
1535579	29177	29193	31243	31259	GTTATTAGATAATTGGG	20	AO	3068
1535592	25066	25082	27132	27148	ACCATATGATGTATCAT	6	AO	3069
1535605	27389	27405	29455	29471	GTTAATAGTTCTCTGTT	9	AO	3070

Example 3: Design and Effect of 4-10-3 cEt gapmers complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 17 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkkddddd kkk; wherein "k" represents a cEt sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified

oligonucleotides is (from 5' to 3'): soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Table 7

4-10-3 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535187	48859	48875	50925	50941	AGGTTTTCATCAATATC	3	AO	3071
1535188	66282	66298	68348	68364	TGTCATATAGTCTCTG	6	AO	3072
1535457	45416	45432	47482	47498	GTAGGTATTATTTGTCA	9	AO	3073
1535458	17436	17452	19502	19518	TTCAAGATATTCATCCA	9	AO	3074
1535459	19587	19603	21653	21669	CGCTGATTCAAGTCACT	12	AO	3075
1535460	18573	18589	20639	20655	GAAAGGTTATCCAGTCA	26	AO	3076
1535461	45127	45143	47193	47209	TCTGATTATATTTTGCC	13	AO	3077
1535463	27490	27506	29556	29572	AGACAATCCATTATTCG	18	AO	3078
1535464	23227	23243	25293	25309	TGTATGTACAACCTCAG	8	AO	3079
1535465	44506	44522	46572	46588	CAAGGATTCACTTTCAG	15	AO	3080
1535466	16695	16711	18761	18777	TACTGTATTAGTTCCAT	3	AO	3081
1535467	21410	21426	23476	23492	GGAAGTATTTGTCTCTA	11	AO	3082
1535468	29227	29243	31293	31309	ATGGATAAAATTCAGAC	23	AO	3083
1535469	33498	33514	35564	35580	GGAGTTTACAATTTGGC	27	AO	3084
1535470	21484	21500	23550	23566	GGATGTATAGTCATGCA	5	AO	3085
1535471	29178	29194	31244	31260	AGTTATTAGATAATTGG	32	AO	3086
1535472	25067	25083	27133	27149	GACCATATGATGTATCA	15	AO	3087
1535475	27390	27406	29456	29472	TGTTAATAGTTCTCTGT	4	AO	3088
1535476	26511	26527	28577	28593	TAAGTTTAAACCAGTGC	8	AO	3089
1535477	19425	19441	21491	21507	AAAGGTATGAACTTCAA	3	AO	3090

1535478	39950	39966	42016	42032	TGAGTTAAGCATTTCAGA	17	AO	3091
1535479	20958	20974	23024	23040	GGGTCATTAGAATTCAC	28	AO	3092
1535480	33040	33056	35106	35122	TGCATAGAGATCCTCTC	4	AO	3093
1535481	17129	17145	19195	19211	AGGTGAATAACACTTTG	11	AO	3094
1535482	45061	45077	47127	47143	TGTTCACTAATATATCC	2	AO	3095
1535483	19935	19951	22001	22017	AGACATTTCAAGCTTAT	7	AO	3096
1535484	19558	19574	21624	21640	TATTCTTAGAACAAGCA	8	AO	3097
1535486	85917	85933	87983	87999	TGCATTAAGTCAATAGG	30	AO	3098
1535487	18632	18648	20698	20714	TTCAACAATTTTCTAGT	21	AO	3099
1535488	48472	48488	50538	50554	CTAGTTATTCTCAGCGG	3	AO	3100
1535489	33024	33040	35090	35106	CGCATAGAGAATTCCTG	15	AO	3101
1535490	16106	16122	18172	18188	AACCGTAATCTCACCAG	4	AO	3102
1535491	21225	21241	23291	23307	ACCATATTGTTCTCAGA	2	AO	3103
1535492	41388	41404	43454	43470	ACTTACAATCATATGCA	19	AO	3104
1535493	33870	33886	35936	35952	TGAGTAGAACACTTTTT	33	AO	3105
1535494	20821	20837	22887	22903	CCAACCTTTACATACCA	5	AO	3106
1535495	26738	26754	28804	28820	AGTATTTTATACACAGC	3	AO	3107
1535497	16666	16682	18732	18748	AGTTATAATATCTTTGG	5	AO	3108
1535498	22512	22528	24578	24594	ATGACAAATACAATTGG	9	AO	3109
1535499	16196	16212	18262	18278	AAAGGTAGCACTTTTTC	6	AO	3110
1535500	17727	17743	19793	19809	AAGCATATTTGTACAA	7	AO	3111
1535501	32744	32760	34810	34826	AGTCTAAAATAGATCTG	18	AO	3112
1535502	35940	35956	38006	38022	GGTGAAATAAAGTTCCT	13	AO	3113
1535503	34755	34771	36821	36837	GGTGAATATCATGTAGC	2	AO	3114
1535504	18736	18752	20802	20818	TCCAGATTTTTTAGCAT	26	AO	3115
1535505	26370	26386	28436	28452	AATAGTTACTTAGTTGC	5	AO	3116
1535506	30209	30225	32275	32291	AAGATTATCTCATGAG	4	AO	3117
1535508	31421	31437	33487	33503	AGGTATTAATTTCAAGC	9	AO	3118
1535509	22620	22636	24686	24702	AATTACTTCATATACGA	10	AO	3119
1535510	22013	22029	24079	24095	GAAAGTAGATTTTAGGC	4	AO	3120
1535511	27932	27948	29998	30014	AGGTAATAAAGTCACGG	9	AO	3121
1535512	41667	41683	43733	43749	GGCAAATATTGTAACCC	11	AO	3122
1535513	18628	18644	20694	20710	ACAATTTTCTAGTAGAG	10	AO	3123
1535514	32178	32194	34244	34260	TGCATTCTAGCTTAGG	14	AO	3124

Example 4: Design and Effect of 4-10-4 cEt gapmers complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 18 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkkddddd kkkk; wherein "k" represents a cEt sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified

oligonucleotides is (from 5' to 3'): soooooooooos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 8

4-10-4 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535191	48858	48875	50924	50941	AGGTTTTCATCAATATCT	45	AQ	3125
1535192	66281	66298	68347	68364	TGTCATATAGTCTCTGG	28	AQ	3126
1535204	31420	31437	33486	33503	AGGTATTAATTTCAAGCT	15	AQ	3127
1535205	22619	22636	24685	24702	AATTACTTCATATACGAG	13	AQ	3128
1535206	22012	22029	24078	24095	GAAAGTAGATTTTAGGCA	12	AQ	3129
1535207	27931	27948	29997	30014	AGGTAATAAAGTCACGGG	15	AQ	3130
1535208	41666	41683	43732	43749	GGCAAATATTGTAACCCC	20	AQ	3131
1535209	18627	18644	20693	20710	ACAATTTTCTAGTAGAGC	6	AQ	3132
1535210	32177	32194	34243	34260	TGCATTCTAGCTTAGGT	5	AQ	3133
1535570	45415	45432	47481	47498	GTAGGTATTATTTGTCAC	9	AQ	3134
1535571	17435	17452	19501	19518	TTCAAGATATTCATCCAA	9	AQ	3135
1535572	19586	19603	21652	21669	CGCTGATTCAAGTCACTT	20	AQ	3136
1535573	18572	18589	20638	20655	GAAAGGTTATCCAGTCAG	13	AQ	3137
1535574	45126	45143	47192	47209	TCTGATTATATTTGCCT	18	AQ	3138
1535575	27489	27506	29555	29572	AGACAATCCATTATTCGT	25	AQ	3139
1535576	23226	23243	25292	25309	TGTATGTACAACCTCAGA	8	AQ	3140
1535577	44505	44522	46571	46588	CAAGGATTCACCTTCAGA	10	AQ	3141
1535578	16694	16711	18760	18777	TACTGTATTAGTTCCATA	4	AQ	3142
1535580	21409	21426	23475	23492	GGAAGTATTTGTCTCTAT	10	AQ	3143
1535581	29226	29243	31292	31309	ATGGATAAAATTCAGACA	5	AQ	3144

1535582	33497	33514	35563	35580	GGAGTTTACAATTTGGCA	25	AQ	3145
1535583	21483	21500	23549	23566	GGATGTATAGTCATGCAT	8	AQ	3146
1535584	29177	29194	31243	31260	AGTTATTAGATAATTGGG	10	AQ	3147
1535585	25066	25083	27132	27149	GACCATATGATGTATCAT	8	AQ	3148
1535586	27389	27406	29455	29472	TGTTAATAGTTCTCTGTT	10	AQ	3149
1535587	26510	26527	28576	28593	TAAGTTTTAACCAGTGCG	12	AQ	3150
1535588	19424	19441	21490	21507	AAAGGTATGAACTTCAAG	7	AQ	3151
1535589	39949	39966	42015	42032	TGAGTTAAGCATTTCAGAT	6	AQ	3152
1535590	20957	20974	23023	23040	GGGTCATTAGAATTCACCT	39	AQ	3153
1535591	33039	33056	35105	35122	TGCATAGAGATCCTCTCG	25	AQ	3154
1535593	17128	17145	19194	19211	AGGTGAATAACACTTTGG	6	AQ	3155
1535594	45060	45077	47126	47143	TGTTCATAACTATATCCA	8	AR	3156
1535595	19934	19951	22000	22017	AGACATTTCAAGCTTATT	3	AR	3157
1535596	19557	19574	21623	21640	TATTCCTAGAACAAGCAG	3	AR	3158
1535597	85916	85933	87982	87999	TGCATTAACCTCAATAGGT	26	AR	3159
1535598	18631	18648	20697	20714	TTCAACAATTTTCTAGTA	9	AR	3160
1535599	48471	48488	50537	50554	CTAGTTATTCTCAGCGGT	5	AR	3161
1535600	33023	33040	35089	35106	CGCATAGAGAATTCCTGC	17	AR	3162
1535601	16105	16122	18171	18188	AACCGTAATCTCACCAGC	10	AR	3163
1535602	21224	21241	23290	23307	ACCATATTGTTCTCAGAG	11	AR	3164
1535603	41387	41404	43453	43470	ACTTACAATCATATGCAC	8	AR	3165
1535604	33869	33886	35935	35952	TGAGTAGAACACTTTTTC	8	AR	3166
1535606	20820	20837	22886	22903	CCAACCTTTACATACCAC	10	AR	3167
1535607	26737	26754	28803	28820	AGTATTTTATACACAGCA	4	AR	3168
1535608	16665	16682	18731	18748	AGTTATAATATCTTTGGT	3	AR	3169
1535609	22511	22528	24577	24594	ATGACAAATACAATTGGC	3	AR	3170
1535610	16195	16212	18261	18278	AAAGGTAGCACTTTTCA	9	AR	3171
1535611	17726	17743	19792	19809	AAGCATATTTTGTACAAA	19	AR	3172
1535612	32743	32760	34809	34826	AGTCTAAAATAGATCTGG	18	AR	3173
1535613	35939	35956	38005	38022	GGTGAAATAAAGTTCCTA	22	AR	3174
1535614	34754	34771	36820	36837	GGTGAATATCATGTAGCA	10	AR	3175
1535615	18735	18752	20801	20818	TCCAGATTTTTCATGATC	27	AR	3176
1535616	26369	26386	28435	28452	AATAGTTACTTAGTTGCA	4	AR	3177
1535617	30208	30225	32274	32291	AAGATTTATCTCATGAGT	3	AR	3178

Example 5: Design and Effect of 5-10-5 cEt gapmers complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

5

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkkkddddd kkkkk; wherein "k" represents a cEt sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified

oligonucleotides is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 9

5-10-5 cEt gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535189	48857	48876	50923	50942	AAGGTTTTTCATCAATATCTG	21	AR	3179
1535190	66280	66299	68346	68365	CTGTCAATATAGTCTCTGGC	46	AR	3180
1535515	45414	45433	47480	47499	TGTAGGTATTATTTGTCACA	16	AR	3181
1535516	17434	17453	19500	19519	TTTCAAGATATTCATCCAAA	16	AR	3182
1535517	19585	19604	21651	21670	ACGCTGATTCAAGTCACTTT	17	AR	3183
1535518	18571	18590	20637	20656	CGAAAGGTTATCCAGTCAGG	8	AR	3184
1535519	45125	45144	47191	47210	TTCTGATTATATTTGCCTA	63	AR	3185
1535520	27488	27507	29554	29573	AAGACAATCCATTATTCGTC	38	AR	3186
1535522	23225	23244	25291	25310	CTGTATGTACAACCTCAGAA	35	AR	3187
1535523	44504	44523	46570	46589	TCAAGGATTCACTTTCAGAA	34	AR	3188
1535524	16693	16712	18759	18778	ATACTGTATTAGTTCATAT	6	AR	3189
1535525	21408	21427	23474	23493	TGGAAGTATTTGTCTCTATA	23	AR	3190
1535526	29225	29244	31291	31310	CATGGATAAAATTCAGACAG	10	AR	3191
1535527	33496	33515	35562	35581	TGGAGTTTACAATTTGGCAG	62	AR	3192
1535528	21482	21501	23548	23567	TGGATGTATAGTCATGCATA	27	AR	3193
1535529	29176	29195	31242	31261	CAGTTATTAGATAATTGGGA	11	AR	3194
1535530	25065	25084	27131	27150	AGACCATATGATGTATCATA	20	AR	3195
1535531	27388	27407	29454	29473	TTGTAAATAGTTCTCTGTTT	8	AR	3196
1535532	26509	26528	28575	28594	ATAAGTTTAAACCAGTGCGG	11	AR	3197
1535533	19423	19442	21489	21508	GAAAGGTATGAACTTCAAGA	6	AR	3198

1535534	39948	39967	42014	42033	TTGAGTTAAGCATTTCAGATA	17	AR	3199
1535535	20956	20975	23022	23041	AGGGTCATTAGAATTCACATA	23	AR	3200
1535536	33038	33057	35104	35123	TTGCATAGAGATCCTCTCGC	14	AR	3201
1535537	17127	17146	19193	19212	AAGGTGAATAACACTTTGGC	30	AR	3202
1535538	45059	45078	47125	47144	TTGTTTCATAACTATATCCAG	25	AR	3203
1535539	19933	19952	21999	22018	CAGACATTTCAAGCTTATTT	5	AR	3204
1535540	19556	19575	21622	21641	ATATTCTTAGAACAAGCAGA	8	AR	3205
1535541	85915	85934	87981	88000	ATGCATTAACCAATAGGTA	42	AR	3206
1535543	18630	18649	20696	20715	CTTCAACAATTTTCTAGTAG	9	AR	3207
1535544	48470	48489	50536	50555	ACTAGTTATTCTCAGCGGTA	26	AR	3208
1535545	33022	33041	35088	35107	TCGCATAGAGAATTCCTGCT	51	AR	3209
1535546	16104	16123	18170	18189	GAACCGTAATCTCACCAGCT	23	AR	3210
1535547	21223	21242	23289	23308	AACCATAATTGTTCTCAGAGA	18	AR	3211
1535548	41386	41405	43452	43471	CACCTACAATCATATGCACT	21	AR	3212
1535549	33868	33887	35934	35953	TTGAGTAGAACACTTTTCT	20	AR	3213
1535550	20819	20838	22885	22904	ACCAACTTTTACATACCACA	28	AR	3214
1535551	26736	26755	28802	28821	TAGTATTTTATACACAGCAT	15	AR	3215
1535552	16664	16683	18730	18749	AAGTTATAATATCTTTGGTA	7	AR	3216
1535553	22510	22529	24576	24595	CATGACAAATACAATTGGCA	13	AR	3217
1535554	16194	16213	18260	18279	TAAAGGTAGCACTTTTTCAC	17	AR	3218
1535555	17725	17744	19791	19810	AAAGCATATTTTGTACAAAG	9	AR	3219
1535556	32742	32761	34808	34827	GAGTCTAAAAATAGATCTGGG	68	AR	3220
1535557	35938	35957	38004	38023	AGGTGAAATAAAGTTCCTAC	79	AR	3221
1535558	34753	34772	36819	36838	GGGTGAATATCATGTAGCAT	24	AR	3222
1535559	18734	18753	20800	20819	ATCCAGATTTTTTAGCATCC	42	AR	3223
1535560	26368	26387	28434	28453	TAATAGTFACTTAGTTGCAA	13	AR	3224
1535561	30207	30226	32273	32292	CAAGATTATCTCATGAGTG	6	AR	3225
1535562	31419	31438	33485	33504	AAGGTATTAATTTCAAGCTA	21	AR	3226
1535564	22618	22637	24684	24703	AAATTACTTCATATACGAGT	9	AR	3227
1535565	22011	22030	24077	24096	AGAAAGTAGATTTTAGGCAC	25	AR	3228
1535566	27930	27949	29996	30015	GAGGTAATAAAGTCACGGGG	81	AR	3229
1535567	41665	41684	43731	43750	AGGCAAATATTGTAAACCCC	47	AR	3230
1535568	18626	18645	20692	20711	AACAATTTTCTAGTAGAGCT	3	AR	3231
1535569	32176	32195	34242	34261	ATGCATTCTAGCTTAGGTC	28	AR	3232

Example 6: Design and effect of modified oligonucleotides complementary to human SNCA RNA

Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

5

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 16 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkdyddddddkkk; wherein "k" represents a cEt sugar moiety, "y" represents a 2'-O-methyl sugar moiety and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside

linkage motif for the modified oligonucleotides is (from 5' to 3'): soosssssssos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine, unless otherwise specified. Non-methylated cytosines are **bolded and underlined**.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 1,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (forward sequence ACGAACCTGAAGCCTAAGAAATATCT, designated herein as SEQ ID NO: 10; reverse sequence GAGCACTTGACAGGATGGAACAT, designated herein as SEQ ID NO: 11; probe sequence TGCTCCCAGTTTCTTGAGATCTGCTGACA, designated herein as SEQ ID NO: 12). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 10

3-10-3 gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1486711	2619	2634	4685	4700	TTTA <u>C</u> ACCACACTGGA	49	AC	17
1486712	2641	2656	4707	4722	ACAT <u>C</u> CATGGCTAATG	43	AC	2483
1486713	2628	2643	4694	4709	ATGAATTCCTTTACAC	53	AC	1635
1486714	2658	2673	4724	4739	AAAGUCCTTTCATGAA	51	AC	3233
1486716	48876	48891	50942	50957	ATTAAGAGGAAGGTAA	59	AC	1177
1486717	2621	2636	4687	4702	CCTTUACACCACACTG	40	AC	3234
1486718	2665	2680	4731	4746	GCCTUTGAAAGTCCTT	27	AC	3235
1486719	2633	2648	4699	4714	GGCTAATGAATTCCTT	27	AC	1944
1486720	2627	2642	4693	4708	TGAAUTCCTTTACACC	30	AC	3236
1486721	2667	2682	4733	4748	TGGC <u>C</u> TTTGAAAGTCC	43	AC	2169
1486722	48861	48876	50927	50942	AAGGUTTTCATCAATA	27	AC	3237
1486723	2659	2674	4725	4740	GAAAGTCCTTTCATGA	46	AC	1713
1486724	2656	2671	4722	4737	AGTC <u>C</u> TTTCATGAATA	27	AC	1479
1486725	2626	2641	4692	4707	GAATUCCTTTACACCA	22	AC	3238
1486726	2668	2683	4734	4749	TTGG <u>C</u> CTTTGAAAGTC	49	AC	2253

1486727	2661	2676	4727	4742	TTGAAAGTCCTTTCAT	77	AC	1867
1486729	48867	48882	50933	50948	AAGGUAAAAGGTTTTCA	82	AC	3239
1486730	48878	48893	50944	50959	GAATUAAGAGGAAGGT	35	AC	3240
1486731	48866	48881	50932	50947	AGGTAAAGGTTTTTCAT	61	AC	2633
1486732	48864	48879	50930	50945	GTAAAGGTTTTTCATCA	28	AC	2481
1486733	48874	48889	50940	50955	TAAGAGGAAGGTAAAG	66	AC	1017
1486734	2635	2650	4701	4716	ATGGCTAATGAATTCC	20	AC	2018
1486735	48850	48865	50916	50931	CAATATCTGCAATAAT	71	AC	1709
1486736	2655	2670	4721	4736	GTCCUTTCATGAATAC	33	AC	3241
1486737	48862	48877	50928	50943	AAAGGTTTTTCATCAAT	37	AC	2401
1486738	2623	2638	4689	4704	TTCCUTTACACCACAC	20	AC	3242
1486739	2620	2635	4686	4701	CTTTACACCACACTGG	56	AC	1016
1486740	2654	2669	4720	4735	TCCTUTCATGAATACA	15	AC	3243
1486741	2646	2661	4712	4727	TGAAUACATCCATGGC	32	AC	3244
1486742	48865	48880	50931	50946	GGTAAAGGTTTTTCATC	58	AC	2560
1486743	2634	2649	4700	4715	TGGCUAATGAATTCCT	43	AC	3245
1486744	2657	2672	4723	4738	AAGTCTTTCATGAAT	41	AC	1555
1486745	2647	2662	4713	4728	ATGAATACATCCATGG	42	AC	21
1486746	48857	48872	50923	50938	TTTTCATCAATATCTG	11	AC	2015
1486747	48845	48860	50911	50926	TCTGCAATAATATTAT	56	AC	1402
1486748	48853	48868	50919	50934	CATCAATATCTGCAAT	30	AC	1865
1486749	2625	2640	4691	4706	AATTCTTTACACCAC	31	AC	1481
1486750	2643	2658	4709	4724	ATACATCCATGGCTAA	25	AC	2638
1486751	2622	2637	4688	4703	TCCTUTACACCACACT	31	AC	3246
1486752	48858	48873	50924	50939	GTTTUCATCAATATCT	20	AC	3247
1486753	48855	48870	50921	50936	TTCAUCAATATCTGCA	39	AC	3248
1486754	2624	2639	4690	4705	ATTCTTTACACCACA	26	AC	1399
1486755	2652	2667	4718	4733	CTTTCATGAATACATC	32	AC	1178
1486756	2648	2663	4714	4729	CATGAATACATCCATG	69	AC	99
1486757	48860	48875	50926	50941	AGGTUTTCATCAATAT	24	AC	3249
1486758	48869	48884	50935	50950	GGAAGGTAAAGGTTTT	33	AC	2864
1486759	2644	2659	4710	4725	AATACATCCATGGCTA	38	AC	2712
1486760	2650	2665	4716	4731	TTCAUGAATACATCCA	27	AC	3250
1486761	2651	2666	4717	4732	TTTCATGAATACATCC	18	AC	1093
1486762	48847	48862	50913	50928	TATCUGCAATAATATT	50	AC	3251
1486763	2663	2678	4729	4744	CTTTGAAAGTCCTTTC	52	AC	1941
1486764	48856	48871	50922	50937	TTTCATCAATATCTGC	17	AC	19
1486765	2642	2657	4708	4723	TACAUCCATGGCTAAT	45	AC	3252
1486766	2660	2675	4726	4741	TGAAAGTCCTTTCATG	66	AC	1790
1486767	2636	2651	4702	4717	CATGGCTAATGAATTC	34	AC	2100
1486768	2666	2681	4732	4747	GGCCUTTGAAGTCCT	43	AC	3253
1486769	2632	2647	4698	4713	GCTAATGAATTCCTTT	19	AC	1863
1486770	48836	48851	50902	50917	ATATUATTAAATTGGG	72	AC	3254
1486771	2631	2646	4697	4712	CTAAUGAATTCCTTTA	65	AC	3255
1486772	48854	48869	50920	50935	TCATCAATATCTGCAA	35	AC	1939

1486773	2640	2655	4706	4721	CATCCATGGCTAATGA	55	AC	2400
1486774	2664	2679	4730	4745	CCTTUGAAAAGTCCTTT	45	AC	3256
1486775	2662	2677	4728	4743	TTTGAAAAGTCCTTTCA	52	AC	3257
1486776	2671	2686	4737	4752	TCCTUGGCCTTTGAAA	81	AC	3258
1486777	48835	48850	50901	50916	TATTATTAAATTGGGC	65	AC	1176
1486778	2637	2652	4703	4718	CCATGGCTAATGAATT	43	AC	2171
1486779	2645	2660	4711	4726	GAATACATCCATGGCT	44	AC	2786
1486780	2639	2654	4705	4720	ATCCATGGCTAATGAA	41	AC	2324
1486782	2638	2653	4704	4719	TCCAUGGCTAATGAAT	62	AC	3259
1486783	48870	48885	50936	50951	AGGAAGGTAAAGGTTT	33	AC	16
1486784	2653	2668	4719	4734	CCTTUCATGAATACAT	36	AC	3260
1486785	2649	2664	4715	4730	TCATGAATACATCCAT	30	AC	943
1486786	48871	48886	50937	50952	GAGGAAGGTAAAGGTT	45	AC	98
1486787	2630	2645	4696	4711	TAATGAATTCCTTTAC	60	AC	1716

Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 3 (GENBANK Accession No: NM_001146055.1), as indicated. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

5

Table 11

3-10-3 gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 3 Start Site	SEQ ID NO: 3 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1486715	42	57	CTTTACACCACACTCT	70	AC	3015
1486728	41	56	TTTACACCACACTCTT	65	AC	938
1486781	43	58	CCTTUACACCACACTC	36	AC	3016

Example 7: Design and Effect of cEt gapmers containing 2'-MOE modifications complementary to human SNCA RNA

10 Modified oligonucleotides complementary to a human SNCA RNA were designed and tested for their single dose effects on SNCA RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

15 "Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (Ensembl Accession ENSG00000145335.17, Ensembl release 106 - Apr 2022) or to SEQ ID NO: 2 (the complement of GENBANK Accession No: NT_016354.20 truncated from nucleoside 30800000 to nucleoside 30919000), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

20 Cultured differentiated SH-SY5Y cells were treated with modified oligonucleotide at a concentration of 2,000 nM by electroporation at a density of 20,000 cells per well. After a treatment period of approximately 24 hours, total RNA

was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. SNCA RNA levels were measured by human primer-probe set RTS2621 (described herein above). SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of SNCA RNA is presented in the table below as percent SNCA RNA relative to the amount of SNCA RNA in untreated control cells (% UTC). Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 17 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkdddddkeee; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 12

cEt gapmers containing 2'-MOE modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535196	48858	48874	50924	50940	GGTTTTTCATCAATATCT	4	AM	3018
1535197	66281	66297	68347	68363	GTCAATATAGTCTCTGG	15	AM	3017
1535268	45415	45431	47481	47497	TAGGTATTATTTGTCAC	35	AM	3060
1535269	17435	17451	19501	19517	TCAAGATATTCATCCAA	14	AM	3019
1535271	19586	19602	21652	21668	GCTGATTCAAGTCACTT	48	AM	3030
1535272	18572	18588	20638	20654	AAAGGTTATCCAGTCAG	27	AM	3041
1535273	45126	45142	47192	47208	CTGATTATATTTGCCT	17	AM	3052
1535274	27489	27505	29555	29571	GACAATCCATTATTCGT	49	AM	3059
1535275	23226	23242	25292	25308	GTATGTACAACCTCAGA	8	AM	3061
1535276	44505	44521	46571	46587	AAGGATTCACTTTCAGA	14	AM	3062
1535277	16694	16710	18760	18776	ACTGTATTAGTTCATA	5	AM	3063
1535278	21409	21425	23475	23491	GAAGTATTTGTCTCTAT	19	AM	3064
1535279	29226	29242	31292	31308	TGGATAAAATTCAGACA	22	AM	3065
1535280	33497	33513	35563	35579	GAGTTTACAATTTGGCA	15	AM	3066
1535282	21483	21499	23549	23565	GATGTATAGTCATGCAT	21	AM	3067
1535283	29177	29193	31243	31259	GTTATTAGATAATTGGG	10	AM	3068
1535284	25066	25082	27132	27148	ACCATATGATGTATCAT	24	AM	3069
1535285	27389	27405	29455	29471	GTTAATAGTTCTCTGTT	19	AM	3070
1535286	26510	26526	28576	28592	AAGTTTTAACCAGTGCG	17	AM	3020
1535287	19424	19440	21490	21506	AAGGTATGAACCTCAAG	7	AM	3021
1535288	39949	39965	42015	42031	GAGTTAAGCATTCAGAT	7	AM	3022
1535289	20957	20973	23023	23039	GGTCATTAGAATTCAT	15	AM	3023
1535290	33039	33055	35105	35121	GCATAGAGATCCTCTCG	7	AM	3024
1535291	17128	17144	19194	19210	GGTGAATAACACTTTGG	18	AM	3025
1535293	45060	45076	47126	47142	GTTCACTAATATATCCA	25	AM	3026

1535294	19934	19950	22000	22016	GACATTTCAAGCTTATT	3	AM	3027
1535295	19557	19573	21623	21639	ATTCTTAGAACAAGCAG	7	AM	3028
1535296	85916	85932	87982	87998	GCATTAACCAATAGGT	48	AM	3029
1535297	18631	18647	20697	20713	TCAACAATTTCTAGTA	14	AM	3031
1535298	48471	48487	50537	50553	TAGTTATTCTCAGCGGT	16	AM	3032
1535299	33023	33039	35089	35105	GCATAGAGAATTCCTGC	10	AM	3033
1535300	16105	16121	18171	18187	ACCGTAATCTCACCAGC	9	AM	3034
1535301	21224	21240	23290	23306	CCATATTGTTCTCAGAG	16	AM	3035
1535302	41387	41403	43453	43469	CTTACAATCATATGCAC	41	AM	3036
1535304	33869	33885	35935	35951	GAGTAGAACACTTTTTC	8	AM	3037
1535305	20820	20836	22886	22902	CAACTTTTACATACCAC	12	AM	3038
1535306	26737	26753	28803	28819	GTATTTTATACACAGCA	9	AM	3039
1535307	16665	16681	18731	18747	GTTATAATATCTTTGGT	20	AM	3040
1535308	22511	22527	24577	24593	TGACAAATACAATTGGC	7	AM	3042
1535309	16195	16211	18261	18277	AAGGTAGCACTTTTCA	35	AM	3043
1535310	17726	17742	19792	19808	AGCATATTTTGTACAAA	18	AM	3044
1535311	32743	32759	34809	34825	GTCTAAATAGATCTGG	22	AM	3045
1535312	35939	35955	38005	38021	GTGAAATAAAGTTCCTA	5	AM	3046
1535313	34754	34770	36820	36836	GTGAATATCATGTAGCA	14	AM	3047
1535316	18735	18751	20801	20817	CCAGATTTTTTAGCATC	9	AM	3048
1535317	26369	26385	28435	28451	ATAGTTACTTAGTTGCA	6	AM	3049
1535318	30208	30224	32274	32290	AGATTTATCTCATGAGT	8	AM	3050
1535319	31420	31436	33486	33502	GGTATTAATTTCAAGCT	19	AM	3051
1535320	22619	22635	24685	24701	ATTACTTCATATACGAG	7	AM	3053
1535321	22012	22028	24078	24094	AAAGTAGATTTTAGGCA	9	AM	3054
1535322	27931	27947	29997	30013	GGTAATAAAGTCACGGG	15	AM	3055
1535323	41666	41682	43732	43748	GCAAATATTGTAACCCC	29	AM	3056
1535324	18627	18643	20693	20709	CAATTTTCTAGTAGAGC	10	AM	3057
1535325	32177	32193	34243	34259	GCATTTCTAGCTTAGGT	7	AM	3058

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 17 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkdddddccccckee; wherein "k" represents a cEt sugar moiety, "c" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 13

cEt gapmers containing 2'-MOE modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535194	48858	48874	50924	50940	GGTTTTTCATCAATATCT	14	AM	3018
1535195	66281	66297	68347	68363	GTCAATATAGTCTCTGG	12	AM	3017
1535211	45415	45431	47481	47497	TAGGTATTATTTGTCAC	9	AM	3060
1535212	17435	17451	19501	19517	TCAAGATATTCATCCAA	14	AM	3019
1535213	19586	19602	21652	21668	GCTGATTCAAGTCACTT	7	AM	3030
1535214	18572	18588	20638	20654	AAAGGTTATCCAGTCAG	5	AM	3041
1535216	45126	45142	47192	47208	CTGATTATATTTGCCT	11	AM	3052
1535217	27489	27505	29555	29571	GACAATCCATTATTCGT	18	AM	3059
1535218	23226	23242	25292	25308	GTATGTACAACCTCAGA	17	AM	3061
1535219	44505	44521	46571	46587	AAGGATTCACCTTCAGA	26	AM	3062
1535220	16694	16710	18760	18776	ACTGTATTAGTTCATA	3	AM	3063
1535221	21409	21425	23475	23491	GAAGTATTTGTCTCTAT	16	AM	3064
1535222	29226	29242	31292	31308	TGGATAAAATTCAGACA	7	AM	3065
1535223	33497	33513	35563	35579	GAGTTTACAATTTGGCA	14	AM	3066
1535224	21483	21499	23549	23565	GATGTATAGTCATGCAT	16	AM	3067
1535225	29177	29193	31243	31259	GTTATTAGATAAATTGGG	6	AM	3068
1535227	25066	25082	27132	27148	ACCATATGATGTATCAT	7	AM	3069
1535228	27389	27405	29455	29471	GTTAATAGTTCTCTGTT	19	AM	3070
1535229	26510	26526	28576	28592	AAGTTTTAACCAGTGCG	11	AM	3020
1535230	19424	19440	21490	21506	AAGGTATGAACCTCAAG	21	AM	3021
1535231	39949	39965	42015	42031	GAGTTAAGCATTCAAGAT	4	AM	3022
1535232	20957	20973	23023	23039	GGTCATTAGAATTCACT	5	AM	3023
1535233	33039	33055	35105	35121	GCATAGAGATCCTCTCG	5	AM	3024
1535234	17128	17144	19194	19210	GGTGAATAACACTTTGG	4	AN	3025
1535235	45060	45076	47126	47142	G TTCATAACTATATCCA	7	AN	3026
1535236	19934	19950	22000	22016	GACATTTCAAGCTTATT	10	AN	3027
1535238	19557	19573	21623	21639	ATTCTTAGAACAAGCAG	5	AN	3028
1535239	85916	85932	87982	87998	GCATTAACTCAATAGGT	11	AN	3029
1535240	18631	18647	20697	20713	TCAACAATTTTCTAGTA	19	AN	3031
1535241	48471	48487	50537	50553	TAGTTATTCTCAGCGGT	3	AN	3032
1535242	33023	33039	35089	35105	GCATAGAGAATTCTCTGC	13	AN	3033
1535243	16105	16121	18171	18187	ACCGTAATCTCACCAGC	10	AN	3034
1535244	21224	21240	23290	23306	CCATATTGTTCTCAGAG	9	AN	3035
1535245	41387	41403	43453	43469	CTTACAATCATATGCAC	23	AN	3036
1535246	33869	33885	35935	35951	GAGTAGAACACTTTTTC	16	AN	3037
1535247	20820	20836	22886	22902	CAACTTTTACATACCAC	6	AN	3038
1535249	26737	26753	28803	28819	GTATTTTATACACAGCA	6	AN	3039
1535250	16665	16681	18731	18747	GTTATAATATCTTTGGT	7	AN	3040
1535251	22511	22527	24577	24593	TGACAAATACAATTGGC	6	AN	3042
1535252	16195	16211	18261	18277	AAGGTAGCACTTTTCA	7	AN	3043

1535253	17726	17742	19792	19808	AGCATATTTTGTACAAA	7	AN	3044
1535254	32743	32759	34809	34825	GTCTAAAAATAGATCTGG	14	AN	3045
1535255	35939	35955	38005	38021	GTGAAATAAAGTTCCTA	5	AN	3046
1535256	34754	34770	36820	36836	GTGAATATCATGTAGCA	7	AN	3047
1535257	18735	18751	20801	20817	CCAGATTTTTTAGCATC	9	AN	3048
1535258	26369	26385	28435	28451	ATAGTTACTTAGTTGCA	3	AN	3049
1535260	30208	30224	32274	32290	AGATTTATCTCATGAGT	6	AN	3050
1535261	31420	31436	33486	33502	GGTATTAATTTCAAGCT	4	AN	3051
1535262	22619	22635	24685	24701	ATTACTTCATATACGAG	11	AN	3053
1535263	22012	22028	24078	24094	AAAGTAGATTTTAGGCA	8	AN	3054
1535264	27931	27947	29997	30013	GGTAATAAAGTCACGGG	21	AN	3055
1535265	41666	41682	43732	43748	GCAAATATTGTAACCCC	13	AN	3056
1535266	18627	18643	20693	20709	CAATTTCTAGTAGAGC	11	AN	3057
1535267	32177	32193	34243	34259	GCATTCTAGCTTAGGT	4	AN	3058

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 18 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkkkkkkkkkkkkkkk; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

10

Table 14

cEt gapmers containing 2'-MOE modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535200	48857	48874	50923	50940	GGTTTTTCATCAATATCTG	6	AP	3261
1535201	66280	66297	68346	68363	GTCAATATAGTCTCTGGC	13	AP	3262
1535383	45414	45431	47480	47497	TAGGTATTATTTGTCACA	3	AP	3263
1535384	17434	17451	19500	19517	TCAAGATATTCATCCAAA	25	AP	3264
1535385	19585	19602	21651	21668	GCTGATTCAAGTCACTTT	8	AP	3265
1535386	18571	18588	20637	20654	AAAGGTTATCCAGTCAGG	14	AP	3266
1535387	45125	45142	47191	47208	CTGATTATATTTGCCTA	20	AP	3267
1535388	27488	27505	29554	29571	GACAATCCATTATTCGTC	21	AP	3268
1535389	23225	23242	25291	25308	GTATGTACAACCTCAGAA	6	AP	3269
1535390	44504	44521	46570	46587	AAGGATTCACTTTCAGAA	17	AP	3270
1535391	16693	16710	18759	18776	ACTGTATTAGTTCCATAT	4	AP	3271
1535393	21408	21425	23474	23491	GAAGTATTTGTCTCTATA	25	AP	3272
1535394	29225	29242	31291	31308	TGGATAAAATTCAGACAG	9	AP	3273
1535395	33496	33513	35562	35579	GAGTTTACAATTTGGCAG	4	AP	3274

1535396	21482	21499	23548	23565	GATGTATAGTCATGCATA	6	AP	3275
1535397	29176	29193	31242	31259	GTTATTAGATAAATTGGGA	15	AP	3276
1535398	25065	25082	27131	27148	ACCATATGATGTATCATA	12	AP	3277
1535399	27388	27405	29454	29471	GTTAATAGTTCTCTGTTT	10	AP	3278
1535400	26509	26526	28575	28592	AAGTTTTAACCAGTGCGG	3	AP	3279
1535401	19423	19440	21489	21506	AAGGTATGAACCTCAAGA	11	AP	3280
1535402	39948	39965	42014	42031	GAGTTAAGCATTCAGATA	6	AP	3281
1535403	20956	20973	23022	23039	GGTCATTAGAATTCACCTA	19	AP	3282
1535404	33038	33055	35104	35121	GCATAGAGATCCTCTCGC	6	AP	3283
1535406	17127	17144	19193	19210	GGTGAATAACACTTTGGC	6	AP	3284
1535407	45059	45076	47125	47142	GTTCATAACTATATCCAG	14	AP	3285
1535408	19933	19950	21999	22016	GACATTTCAAGCTTATTT	6	AP	3286
1535409	19556	19573	21622	21639	ATTCTTAGAACAAGCAGA	9	AP	3287
1535410	85915	85932	87981	87998	GCATTAACCTCAATAGGTA	17	AP	3288
1535411	18630	18647	20696	20713	TCAACAATTTTCTAGTAG	14	AP	3289
1535412	48470	48487	50536	50553	TAGTTATTCTCAGCGGTA	3	AP	3290
1535413	33022	33039	35088	35105	GCATAGAGAATTCCTGCT	8	AP	3291
1535414	16104	16121	18170	18187	ACCGTAATCTCACCAGCT	6	AP	3292
1535415	21223	21240	23289	23306	CCATATTGTTCTCAGAGA	5	AP	3293
1535416	41386	41403	43452	43469	CTTACAATCATATGCACT	18	AP	3294
1535417	33868	33885	35934	35951	GAGTAGAACACTTTTCT	9	AP	3295
1535419	20819	20836	22885	22902	CAACTTTTACATAACCACA	24	AP	3296
1535420	26736	26753	28802	28819	GTATTTTATACACAGCAT	3	AP	3297
1535421	16664	16681	18730	18747	GTTATAATATCTTTGGTA	3	AP	3298
1535422	22510	22527	24576	24593	TGACAAATACAATTGGCA	8	AP	3299
1535423	16194	16211	18260	18277	AAGGTAGCACTTTTTCAC	14	AP	3300
1535424	17725	17742	19791	19808	AGCATATTTTGTACAAAG	5	AP	3301
1535425	32742	32759	34808	34825	GTCTAAAATAGATCTGGG	9	AP	3302
1535426	35938	35955	38004	38021	GTGAAATAAAGTTCCTAC	18	AP	3303
1535427	34753	34770	36819	36836	GTGAATATCATGTAGCAT	8	AP	3304
1535428	18734	18751	20800	20817	CCAGATTTTCTAGCATCC	3	AP	3305
1535429	26368	26385	28434	28451	ATAGTTACTTAGTTGCAA	7	AP	3306
1535430	30207	30224	32273	32290	AGATTTATCTCATGAGTG	6	AP	3307
1535432	31419	31436	33485	33502	GGTATTAATTTCAAGCTA	14	AP	3308
1535433	22618	22635	24684	24701	ATTACTTCATATACGAGT	6	AP	3309
1535434	22011	22028	24077	24094	AAAGTAGATTTTAGGCAC	21	AP	3310
1535435	27930	27947	29996	30013	GGTAATAAAGTCACGGGG	38	AP	3311
1535436	41665	41682	43731	43748	GCAAATATTGTAACCCCC	9	AP	3312
1535437	18626	18643	20692	20709	CAATTTTCTAGTAGAGCT	5	AP	3313
1535438	32176	32193	34242	34259	GCATTTCTAGCTTAGGTC	7	AP	3314

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 18 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): ekkdddddddddkeeee; wherein "k" represents a cEt sugar

moiety, “e” represents a 2’-MOE sugar moiety, and “d” represents a 2’-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5’ to 3’): soosssssssssssss; wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

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Table 15

cEt gapmers containing 2’-MOE modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535618	32742	32759	34808	34825	GTCTAAAATAGATCTGGG	5	AO	3302
1535619	35938	35955	38004	38021	GTGAAATAAAGTCCTAC	17	AO	3303
1535620	34753	34770	36819	36836	GTGAATATCATGTAGCAT	10	AO	3304
1535621	18734	18751	20800	20817	CCAGATTTTTTAGCATCC	14	AO	3305
1535622	26368	26385	28434	28451	ATAGTTACTTAGTTGCAA	6	AO	3306
1535623	30207	30224	32273	32290	AGATTTATCTCATGAGTG	7	AO	3307
1535624	31419	31436	33485	33502	GGTATTAATTTCAAGCTA	11	AO	3308
1535625	22011	22028	24077	24094	AAAGTAGATTTTAGGCAC	7	AO	3310
1535626	27488	27505	29554	29571	GACAATCCATTATTCGTC	27	AO	3268
1535627	41665	41682	43731	43748	GCAAATATTGTAACCCCC	17	AO	3312
1535628	18626	18643	20692	20709	CAATTTTCTAGTAGAGCT	15	AO	3313
1535629	16693	16710	18759	18776	ACTGTATTAGTTCCATAT	18	AO	3271
1535630	29225	29242	31291	31308	TGGATAAAATTCAGACAG	27	AO	3273
1535631	21482	21499	23548	23565	GATGTATAGTCATGCATA	18	AO	3275
1535632	29176	29193	31242	31259	GTTATTAGATAATTGGGA	10	AO	3276
1535633	25065	25082	27131	27148	ACCATATGATGTATCATA	21	AP	3277
1535634	45414	45431	47480	47497	TAGGTATTATTTGTCACA	11	AP	3263
1535635	27388	27405	29454	29471	GTTAATAGTTCTCTGTTT	9	AP	3278
1535636	26509	26526	28575	28592	AAGTTTTAACCAGTGC GG	5	AP	3279
1535637	33038	33055	35104	35121	GCATAGAGATCCTCTCGC	9	AP	3283
1535638	17127	17144	19193	19210	GGTGAATAACACTTTGGC	5	AP	3284
1535639	45059	45076	47125	47142	GTTCACTAATATATCCAG	16	AP	3285
1535640	85915	85932	87981	87998	GCATTAACCTCAATAGGTA	17	AP	3288
1535641	33022	33039	35088	35105	GCATAGAGAATTCCTGCT	19	AP	3291
1535642	21223	21240	23289	23306	CCATATTGTTCTCAGAGA	7	AP	3293
1535643	33868	33885	35934	35951	GAGTAGAACACTTTTCT	8	AP	3295
1535644	26736	26753	28802	28819	GTATTTTATACACAGCAT	4	AP	3297
1535645	45125	45142	47191	47208	CTGATTATATTTGCCTA	12	AP	3267
1535646	16664	16681	18730	18747	GTTATAATATCTTTGGTA	3	AP	3298
1535647	17725	17742	19791	19808	AGCATATTTGTACAAAG	5	AP	3301

The modified oligonucleotides in the table below are modified oligonucleotides with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 18 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): kkkdddddskkk; wherein "k" represents a cEt sugar moiety, "e" represents a 2'-MOE sugar moiety, and "d" represents a 2'-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soossssssoos; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 16

10 cEt gapmers containing 2'-MOE modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	SNCA RNA (% UTC)	AID	SEQ ID NO
1535198	48857	48874	50923	50940	GGTTTTTCATCAATATCTG	15	AP	3261
1535199	66280	66297	68346	68363	GTCAATATAGTCTCTGGC	11	AP	3262
1535326	45414	45431	47480	47497	TAGGTATTATTTGTCACA	5	AP	3263
1535328	17434	17451	19500	19517	TCAAGATATTCATCCAAA	12	AP	3264
1535329	19585	19602	21651	21668	GCTGATTCAAGTCACTTT	5	AP	3265
1535330	18571	18588	20637	20654	AAAGGTTATCCAGTCAGG	4	AP	3266
1535331	45125	45142	47191	47208	CTGATTATATTTGCCTA	11	AP	3267
1535332	27488	27505	29554	29571	GACAATCCATTATTCGTC	11	AP	3268
1535333	23225	23242	25291	25308	GTATGTACAACCTCAGAA	24	AQ	3269
1535334	44504	44521	46570	46587	AAGGATTCACTTTCAGAA	30	AQ	3270
1535335	16693	16710	18759	18776	ACTGTATTAGTTCCATAT	12	AQ	3271
1535336	21408	21425	23474	23491	GAAGTATTTGTCTCTATA	33	AQ	3272
1535337	29225	29242	31291	31308	TGGATAAAATTCAGACAG	21	AQ	3273
1535338	33496	33513	35562	35579	GAGTTTACAATTTGGCAG	9	AQ	3274
1535339	21482	21499	23548	23565	GATGTATAGTCATGCATA	18	AQ	3275
1535341	29176	29193	31242	31259	GTTATTAGATAAATTGGGA	23	AQ	3276
1535342	25065	25082	27131	27148	ACCATATGATGTATCATA	22	AQ	3277
1535343	27388	27405	29454	29471	GTTAATAGTTCTCTGTTT	11	AQ	3278
1535344	26509	26526	28575	28592	AAGTTTTAACCAGTGCGG	6	AQ	3279
1535345	19423	19440	21489	21506	AAGGTATGAACCTCAAGA	16	AQ	3280
1535346	39948	39965	42014	42031	GAGTTAAGCATTTCAGATA	14	AQ	3281
1535347	20956	20973	23022	23039	GGTCATTAGAATTCACATA	20	AQ	3282
1535348	33038	33055	35104	35121	GCATAGAGATCCTCTCGC	15	AQ	3283
1535349	17127	17144	19193	19210	GGTGAATAACACTTTGGC	3	AQ	3284
1535350	45059	45076	47125	47142	GTTCAATACTATATCCAG	16	AQ	3285
1535351	19933	19950	21999	22016	GACATTTCAAGCTTATTT	12	AQ	3286
1535352	19556	19573	21622	21639	ATTCTTAGAACAAGCAGA	9	AQ	3287
1535354	85915	85932	87981	87998	GCATTAACCTCAATAGGTA	18	AQ	3288
1535355	18630	18647	20696	20713	TCAACAATTTTCTAGTAG	17	AQ	3289
1535356	48470	48487	50536	50553	TAGTTATTCTCAGCGGTA	30	AQ	3290

1535357	33022	33039	35088	35105	GCATAGAGAATTCCTGCT	30	AQ	3291
1535358	16104	16121	18170	18187	ACCGTAATCTCACCAGCT	24	AQ	3292
1535359	21223	21240	23289	23306	CCATATGTTCTCAGAGA	9	AQ	3293
1535360	41386	41403	43452	43469	CTTACAATCATATGCACT	14	AQ	3294
1535361	33868	33885	35934	35951	GAGTAGAACACTTTTCT	48	AQ	3295
1535362	20819	20836	22885	22902	CAACTTTTACATACCACA	23	AQ	3296
1535363	26736	26753	28802	28819	GTATTTTATACACAGCAT	3	AQ	3297
1535364	16664	16681	18730	18747	GTTATAATATCTTTGGTA	8	AQ	3298
1535365	22510	22527	24576	24593	TGACAAATACAATTGGCA	10	AQ	3299
1535367	16194	16211	18260	18277	AAGGTAGCACTTTTTCAC	29	AQ	3300
1535368	17725	17742	19791	19808	AGCATATTTTGTACAAAG	26	AQ	3301
1535369	32742	32759	34808	34825	GTCTAAAATAGATCTGGG	26	AQ	3302
1535370	35938	35955	38004	38021	GTGAAATAAAGTTCCTAC	25	AQ	3303
1535371	34753	34770	36819	36836	GTGAATATCATGTAGCAT	10	AQ	3304
1535372	18734	18751	20800	20817	CCAGATTTTTTAGCATCC	9	AQ	3305
1535373	26368	26385	28434	28451	ATAGTTACTTAGTTGCAA	18	AQ	3306
1535374	30207	30224	32273	32290	AGATTATCTCATGAGTG	7	AQ	3307
1535375	31419	31436	33485	33502	GGTATTAATTTCAAGCTA	14	AQ	3308
1535376	22618	22635	24684	24701	ATTACTTCATATACGAGT	16	AQ	3309
1535377	22011	22028	24077	24094	AAAGTAGATTTTAGGCAC	7	AQ	3310
1535378	27930	27947	29996	30013	GGTAATAAAGTCACGGGG	33	AQ	3311
1535380	41665	41682	43731	43748	GCAAATATTGTAACCCCC	11	AQ	3312
1535381	18626	18643	20692	20709	CAATTTTCTAGTAGAGCT	24	AQ	3313
1535382	32176	32193	34242	34259	GCATTTCTAGCTTAGGTC	8	AQ	3314

Example 8: Dose-dependent inhibition of human SNCA in SH-SY5Y cells by modified oligonucleotides, *in vitro*

Modified oligonucleotides selected from the example above were tested at various doses in SH-SY5Y cells. SH-SY5Y cells plated at a density of 20,000 cells per well were treated using electroporation with various concentrations of modified oligonucleotide as specified in the tables below. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. Human primer-probe set hSNCA_LTS00672_MGB (forward sequence TGGCAGAAGCAGCAGGAAA, designated herein as SEQ ID NO: 3339; reverse sequence TCCTTGGTTTTGGAGCCTACA, designated herein as SEQ ID NO: 3340; probe sequence CAAAAGAGGGTGTCTC, designated herein as SEQ ID NO: 3341) was used to measure RNA levels as described above. SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®.

Reduction of SNCA RNA is presented in the tables below as percent SNCA RNA, relative to the amount of SNCA RNA in untreated control cells (% UTC). The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the table below. Each table represents a separate experiment. Compound No. 1483842 was included in the following experiments as a benchmark.

Table 17

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1483741	87	42	19	9	0.07
1483842	93	73	38	16	0.16
1484502	74	52	28	7	0.07
1484579	79	47	22	9	0.07
1485060	88	55	27	11	0.10
1485169	89	74	37	22	0.17
1485502	78	54	29	13	0.08
1485504	91	61	32	14	0.12
1485587	76	53	35	10	0.08
1485604	96	74	39	20	0.18
1486004	92	71	44	24	0.20
1486159	88	61	31	14	0.11
1486208	81	53	32	22	0.10
1486222	125	96	44	20	0.28
1486366	101	73	43	23	0.21
1486367	75	56	41	16	0.10
1486424	77	38	24	10	0.05
1486654	83	66	37	20	0.14
1486673	96	70	34	17	0.16

Table 18

5 Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482442	92	79	21	12	0.13
1482973	96	79	42	24	0.22
1483553	85	63	32	16	0.12
1483842	105	82	33	24	0.21
1484515	110	101	44	22	0.28
1484558	99	76	35	19	0.18
1484608	93	68	49	20	0.19
1484635	76	64	37	33	0.15
1484827	88	87	44	26	0.24
1484870	107	95	47	21	0.28
1485062	112	91	50	30	0.34
1485624	92	82	51	27	0.28
1485656	98	80	50	46	0.50
1485778	74	69	44	24	0.16
1485869	97	81	43	44	0.40

1486128	90	80	48	38	0.34
1486213	94	87	48	18	0.23
1486485	89	72	45	25	0.20
1486592	3	4	122	1	0.17

Table 19

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1483106	89	71	35	14	0.14
1483775	84	65	26	12	0.10
1483842	91	83	45	21	0.22
1484707	89	67	35	10	0.13
1484757	70	43	24	10	0.05
1484952	94	65	31	12	0.13
1485013	82	57	29	20	0.10
1485018	85	56	38	8	0.11
1485108	83	79	36	12	0.15
1485213	82	51	27	12	0.08
1485540	89	63	26	10	0.11
1485560	93	61	29	13	0.12
1485573	98	77	39	14	0.17
1485671	95	88	36	21	0.20
1485973	71	62	32	12	0.09
1486068	70	38	19	13	0.04
1486348	78	42	18	8	0.06
1486530	71	39	13	8	0.04
1486531	86	56	23	12	0.09

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Table 20

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482396	87	55	26	7	0.09
1483214	80	53	29	15	0.09
1483842	84	73	31	14	0.13
1484242	78	61	25	20	0.10
1484518	70	54	29	12	0.07
1484777	81	61	36	11	0.11
1485389	76	50	23	9	0.07
1485638	84	55	18	7	0.08
1485723	93	80	36	14	0.17

1486093	82	60	25	14	0.09
1486190	67	66	32	15	0.09
1486236	73	47	27	10	0.06
1486251	68	53	30	18	0.07
1486278	80	63	34	23	0.12
1486675	58	34	19	8	0.02
1486740	64	55	29	17	0.06
1486746	71	50	25	9	0.06
1486761	87	60	45	16	0.14
1486764	64	44	14	9	0.04

Table 21

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1483531	92	73	58	21	0.24
1483714	81	60	20	12	0.09
1483842	78	74	33	15	0.13
1484593	87	68	42	16	0.15
1484714	92	70	24	11	0.12
1484754	90	69	25	10	0.12
1484876	107	74	37	16	0.18
1485088	90	90	35	16	0.19
1485220	97	82	56	19	0.26
1485236	65	64	30	13	0.08
1485276	72	61	37	15	0.10
1485431	94	100	37	27	0.27
1485448	111	53	21	19	0.13
1485531	76	62	25	7	0.08
1485660	89	73	34	14	0.15
1485823	91	66	33	21	0.15
1485885	82	71	41	15	0.14
1486089	119	73	35	12	0.18
1486413	93	59	20	12	0.10

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Table 22

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482290	127	97	51	22	0.32
1482708	84	86	38	20	0.19
1483241	83	39	24	6	0.06

1483842	75	72	33	15	0.12
1484583	74	62	31	19	0.10
1484587	86	84	31	24	0.18
1484654	74	96	35	33	0.26
1484742	89	91	34	24	0.21
1484762	69	58	28	8	0.07
1485005	93	97	48	21	0.27
1485651	129	96	33	30	0.29
1485755	105	110	49	15	0.28
1485873	101	77	49	27	0.26
1486125	72	82	38	25	0.17
1486321	117	92	45	14	0.24
1486441	67	74	54	27	0.22
1486515	108	72	29	15	0.18
1486590	76	83	61	42	0.71
1486704	103	70	14	11	0.12

Table 23

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482194	93	58	41	8	0.13
1483367	91	64	22	9	0.11
1483842	88	79	26	23	0.16
1484676	122	60	42	12	0.18
1484743	108	99	47	29	0.34
1484818	108	76	38	15	0.19
1484874	90	53	31	14	0.11
1484882	88	48	27	10	0.09
1485135	77	74	33	18	0.13
1485179	101	76	44	16	0.20
1485242	62	55	25	9	0.05
1485790	96	37	18	11	0.08
1485948	79	77	35	25	0.16
1485988	100	77	40	29	0.23
1486065	94	47	43	11	0.12
1486245	90	69	33	12	0.13
1486253	92	69	30	21	0.15
1486302	74	44	20	24	0.06
1486576	85	82	36	17	0.17

Table 24

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482715	79	91	53	25	0.29
1483673	71	57	46	26	0.12
1483842	78	66	31	20	0.11
1483923	82	45	20	15	0.07
1484542	97	71	35	12	0.15
1484747	96	72	37	23	0.18
1484792	64	72	42	22	0.13
1484797	92	48	39	34	0.16
1484893	97	79	40	16	0.19
1485008	75	65	47	15	0.13
1485484	72	51	35	7	0.07
1485509	90	78	53	30	0.29
1485559	94	54	33	14	0.12
1485636	110	81	64	17	0.30
1485746	88	53	41	17	0.12
1486153	95	91	59	32	0.42
1486181	88	58	55	33	0.23
1486445	98	63	30	21	0.15
1486641	94	98	67	30	0.50

Table 25

5 Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482184	86	71	45	17	0.17
1482400	80	55	37	22	0.11
1483812	59	45	20	23	0.03
1483842	80	70	36	18	0.13
1483984	86	72	36	14	0.14
1484214	90	71	40	18	0.16
1484307	93	52	26	15	0.10
1484793	84	61	30	22	0.12
1485306	86	75	54	36	0.35
1485518	100	91	61	42	0.62
1485569	89	56	30	23	0.12
1485672	76	81	46	20	0.18
1485758	93	80	52	23	0.25
1485858	74	41	29	9	0.06

1485900	94	75	39	24	0.19
1485915	84	62	46	21	0.16
1486282	85	57	31	27	0.13
1486339	64	47	20	21	0.04
1486455	66	45	25	15	0.05

Table 26

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482283	58	33	19	10	0.020
1482427	78	55	24	29	0.10
1483058	90	76	46	19	0.20
1483333	75	52	31	33	0.10
1483785	80	62	45	36	0.22
1483842	78	63	34	39	0.17
1484541	70	63	26	35	0.11
1484842	88	67	32	14	0.13
1484881	77	60	32	16	0.10
1484927	88	76	47	30	0.25
1485251	108	95	69	37	0.60
1485340	85	56	39	20	0.13
1485553	93	56	42	18	0.14
1485701	85	62	33	13	0.11
1485776	86	78	55	48	0.70
1486051	92	64	38	35	0.21
1486110	83	61	34	36	0.17
1486171	82	75	39	44	0.31
1486217	85	67	48	23	0.19

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Table 27

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482394	67	60	26	11	0.07
1483094	73	56	39	15	0.09
1483121	81	55	24	13	0.08
1483453	91	76	38	14	0.16
1483728	70	51	41	10	0.07
1483842	82	76	33	17	0.14
1484616	98	84	55	28	0.32
1484723	73	67	41	18	0.12

1485026	83	43	29	8	0.07
1485044	93	72	44	16	0.17
1485136	69	66	35	17	0.10
1485331	97	75	34	14	0.16
1485433	78	57	21	10	0.08
1485547	77	57	34	20	0.10
1485878	89	48	19	16	0.08
1485947	91	81	41	13	0.17
1486360	86	73	35	21	0.16
1486466	76	51	25	8	0.07
1486642	97	64	32	13	0.13

Table 28

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482633	73	64	27	48	0.18
1482920	77	56	40	12	0.10
1483134	73	54	30	13	0.07
1483717	84	64	44	23	0.16
1483842	86	70	45	21	0.17
1483983	91	74	31	27	0.18
1484220	68	59	52	14	0.11
1484229	84	74	49	24	0.21
1484352	70	65	30	34	0.12
1484512	88	55	32	9	0.10
1484624	72	60	29	12	0.08
1484645	73	54	35	25	0.09
1484671	96	94	52	32	0.38
1485077	98	80	66	31	0.42
1485166	74	46	26	8	0.06
1485206	109	81	46	20	0.24
1485893	76	61	37	23	0.12
1485916	72	70	46	15	0.13
1486602	88	72	46	25	0.21

5

Table 29

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	16 nM	63 nM	250 nM	1000 nM	
1482595	65	50	32	16	0.06
1482916	58	45	16	18	0.03

1483423	61	45	48	18	0.06
1483635	54	40	20	7	0.02
1483842	84	62	28	11	0.10
1484195	88	53	46	18	0.14
1484296	86	69	44	33	0.23
1484895	70	55	42	25	0.10
1485098	81	63	32	11	0.10
1485281	80	58	34	17	0.10
1485351	90	67	33	20	0.14
1485657	94	69	28	15	0.13
1485685	91	81	52	23	0.25
1485980	85	76	45	22	0.20
1486071	68	57	33	19	0.08
1486230	76	61	45	14	0.12
1486434	87	57	33	14	0.11
1486591	61	50	34	10	0.05
1486622	94	88	52	28	0.31

Modified oligonucleotides selected from the example above were tested at various doses in SH-SY5Y cells. SH-SY5Y cells plated at a density of 20,000 cells per well were treated using electroporation with various concentrations of modified oligonucleotide as specified in the tables below. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and SNCA RNA levels were measured by quantitative real-time RT-PCR. Human SNCA primer-probe set RTS2621 (described herein above) was used to measure RNA levels as described above. SNCA RNA levels were normalized to total RNA content, as measured by RIBOGREEN®.

Reduction of SNCA RNA is presented in the tables below as percent SNCA RNA, relative to the amount of SNCA RNA in untreated control cells (% UTC). The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the table below. Each table represents a separate experiment. Compound No. 1486339 was included in the following experiments as a benchmark.

Table 30

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1486339	93	43	48	4	0.21
1535383	97	69	22	5	0.23
1535400	97	64	16	12	0.22
1535412	120	75	35	10	0.36
1535420	87	50	50	7	0.23
1535428	83	36	21	11	0.12
1535466	71	50	30	8	0.13
1535475	78	52	30	39	0.24

1535480	83	59	28	17	0.21
1535488	68	39	31	6	0.09
1535490	104	58	39	14	0.30
1535494	103	56	29	9	0.24
1535495	60	33	11	8	0.05
1535505	80	53	12	7	0.13
1535506	77	42	22	7	0.11
1535510	70	40	26	16	0.10
1535521	75	50	22	5	0.12
1535618	92	81	40	14	0.35
1535646	112	76	32	7	0.33

Table 31

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1482506	95	74	39	34	0.48
1483282	112	69	40	23	0.42
1483576	94	76	43	34	0.55
1486339	86	47	13	8	0.14
1533179	84	51	26	26	0.20
1533225	97	85	66	30	0.86
1533306	102	51	31	8	0.23
1533375	110	76	23	41	0.49
1533391	83	60	42	33	0.37
1533711	94	54	20	15	0.2
1533869	105	88	64	11	0.54
1534076	86	66	47	17	0.32
1534231	83	53	22	18	0.17
1534300	109	92	54	26	0.67
1534348	95	75	40	11	0.32
1534381	91	63	42	38	0.48
1534391	86	77	60	27	0.60
1534409	79	67	44	27	0.34
1534428	95	60	59	11	0.35

5

Table 32

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1482343	95	77	43	17	0.38

1486339	90	47	38	13	0.21
1533267	83	57	26	10	0.18
1533559	78	44	17	26	0.13
1535187	79	60	49	11	0.24
1535196	74	49	21	6	0.12
1535214	88	53	30	15	0.20
1535220	94	56	19	10	0.20
1535231	79	52	20	12	0.14
1535232	97	57	33	22	0.29
1535233	106	59	29	18	0.29
1535277	97	42	29	7	0.18
1535294	100	62	25	8	0.24
1535312	87	70	49	35	0.57
1535317	94	56	27	8	0.21
1535477	76	59	43	14	0.22
1535482	91	62	39	12	0.26
1535491	102	48	28	19	0.24
1535503	78	69	10	46	0.26

Table 33

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1486339	81	59	28	4	0.17
1535209	93	51	33	13	0.22
1535210	100	61	32	26	0.33
1535326	77	48	25	16	0.14
1535330	118	71	43	22	0.45
1535344	97	70	48	19	0.40
1535349	87	58	34	12	0.22
1535363	75	47	40	10	0.15
1535391	76	48	38	13	0.16
1535395	74	54	25	9	0.14
1535415	88	64	43	11	0.27
1535421	79	47	22	7	0.13
1535578	77	59	29	12	0.18
1535581	91	51	31	12	0.20
1535589	93	63	36	21	0.30
1535595	69	42	13	14	0.08
1535596	85	63	20	9	0.18
1535608	62	30	14	4	0.05
1535644	85	59	23	23	0.21

Table 34

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1483398	95	64	23	21	0.26
1483488	80	53	22	14	0.16
1483650	75	47	13	11	0.11
1484024	85	63	25	6	0.19
1486339	75	49	22	6	0.12
1533437	89	66	26	11	0.23
1533457	75	42	28	10	0.12
1533595	74	41	17	5	0.10
1533861	65	37	23	14	0.07
1534379	85	39	13	11	0.12
1534424	75	44	21	9	0.11
1534442	56	36	15	7	0.04
1535539	89	52	30	7	0.19
1535568	86	60	33	9	0.21
1535599	66	27	8	4	0.05
1535607	98	67	33	10	0.27
1535609	88	55	26	15	0.20
1535616	91	87	50	15	0.44
1535617	74	64	23	6	0.16

Table 35

5 Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1482308	66	29	10	6	0.06
1483319	62	37	12	7	0.06
1486339	69	35	16	3	0.07
1533281	71	32	13	7	0.07
1533349	74	38	11	4	0.08
1533965	54	37	11	5	0.04
1534021	51	17	7	5	0.02
1535203	83	51	23	9	0.16
1535234	52	29	15	3	0.03
1535241	83	57	31	8	0.19
1535258	105	75	47	23	0.47
1535267	94	84	28	14	0.32
1535281	84	60	29	11	0.20
1535327	83	59	34	14	0.21

1535446	108	78	36	14	0.37
1535448	61	30	11	5	0.05
1535456	79	54	19	9	0.14
1535473	88	61	27	8	0.20
1535474	61	19	16	4	0.03

Table 36

Dose-dependent reduction of human SNCA RNA in SH-SY5Y cells by modified oligonucleotides

Compound No.	SNCA RNA (% UTC)				IC ₅₀ (μM)
	31 nM	125 nM	500 nM	2000 nM	
1486339	78	47	18	6	0.12
1533013	85	63	34	10	0.22
1533113	94	61	28	10	0.23
1533161	91	74	49	16	0.38
1533215	84	62	24	14	0.20
1533429	87	68	37	20	0.30
1533707	94	63	44	24	0.36
1533919	67	45	13	4	0.08
1533941	86	62	32	25	0.27
1533998	85	50	23	7	0.16
1534005	90	62	31	20	0.26
1534083	89	79	49	24	0.47
1535255	91	65	45	14	0.31
1535261	83	56	32	8	0.19
1535270	79	50	34	8	0.16
1535418	68	36	11	5	0.07
1535431	69	42	11	5	0.08
1535440	71	37	11	9	0.08

5 **Example 9: Design of modified oligonucleotides complementary to human SNCA RNA**

Modified oligonucleotides complementary to a human SNCA RNA were designed as described in the tables below.

10 “Start site” indicates the 5’-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. “Stop site” indicates the 3’-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (described herein above), or to SEQ ID NO: 2 (described herein above), or to both. ‘N/A’ indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

15 The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with uniform phosphorothioate internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeeeeeeeeeeeeeee; wherein each “e” represents a 2’-MOE

sugar moiety and each “d” represents a 2’-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5’ to 3’): sssssssssssssss; wherein each “s” represents a phosphorothioate internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 37

5 5-10-5 MOE gapmers with uniform phosphorothioate linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
789291	2624	2643	4690	4709	ATGAATTCCTTTACACCACA	3315
1523524	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	3316
1523526	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	3317
1601261	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	3318
1601266	46675	46694	48741	48760	ACGACATTTCTTGCCTCTT	3319
1601271	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	3320

The modified oligonucleotides in the table below are 6-10-4 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeeeeeeeeeee; wherein each “e” represents a 2’-MOE sugar moiety and each “d” represents a 2’-β-D-deoxyribose sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5’ to 3’): soooooosssssssoss; wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

10

Table 38

6-10-4 MOE gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
1620589	2624	2643	4690	4709	ATGAATTCCTTTACACCACA	3315
1620591	26390	26409	28456	28475	CAGACTGTAATCTAGGACCC	3321
1620593	46677	46696	48743	48762	TCACGACATTTCTTGCCTC	3322
1620595	2623	2642	4689	4708	TGAATTCCTTTACACCACAC	3323
1620596	46674	46693	48740	48759	CGACATTTCTTGCCTCTTA	3324
1620598	46676	46695	48742	48761	CACGACATTTCTTGCCTCT	3325
1620599	26392	26411	28458	28477	TCCAGACTGTAATCTAGGAC	3326
1620603	46679	46698	48745	48764	CATCACGACATTTCTTGCC	3327
1620604	46675	46694	48741	48760	ACGACATTTCTTGCCTCTT	3319
1620605	46678	46697	48744	48763	ATCACGACATTTCTTGCCT	3328
1620633	26391	26410	28457	28476	CCAGACTGTAATCTAGGACC	3329
1620634	26389	26408	28455	28474	AGACTGTAATCTAGGACCCA	3330
1620635	26393	26412	28459	28478	ATCCAGACTGTAATCTAGGA	3331

5 The modified oligonucleotides in the table below are MOE gapmers with cEt modifications with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeddddddckee; wherein each "e" represents a 2'-MOE sugar moiety, each "k" represents a cEt sugar moiety, and each "d" represents a 2'-β-D-deoxyribsyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): soooooosssssssoss; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

10

Table 39

MOE gapmers with cEt modifications with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
1606563	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	3316
1606564	46675	46694	48741	48760	ACGACATTTTCTTGCCTCTT	3319
1606566	26390	26409	28456	28475	CAGACTGTAATCTAGGACCC	3321
1606568	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	3320
1606571	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	3318
1606572	2624	2643	4690	4709	ATGAATTCCTTTACACCACA	3315
1606573	2623	2642	4689	4708	TGAATTCCTTTACACCACAC	3323

15 The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeedddddddeee; wherein each "e" represents a 2'-MOE sugar moiety and each "d" represents a 2'-β-D-deoxyribsyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): ssssszzzzssssssss; wherein each "s" represents a phosphorothioate internucleoside linkage and each "z" represents a mesyl phosphoramidate internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

20

Table 40

5-10-5 MOE gapmers with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
1601252	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	3316
1601260	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	3318
1601263	2624	2643	4690	4709	ATGAATTCCTTTACACCACA	3315
1601265	46675	46694	48741	48760	ACGACATTTTCTTGCCTCTT	3319
1601268	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	3317
1601270	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	3320

The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "e" represents a 2'-MOE sugar moiety and each "d" represents a 2'-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sooszzzzsssssooss; wherein each "s" represents a phosphorothioate internucleoside linkage, each "z" represents a mesyl phosphoramidate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 41

5-10-5 MOE gapmers with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
1601262	2624	2643	4690	4709	ATGAATTCCTTTACACCACA	3315
1601264	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	3319
1601267	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	3317
1601269	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	3320

The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "e" represents a 2'-MOE sugar moiety and each "d" represents a 2'-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motifs for the modified oligonucleotides are presented in the column labeled "Internucleoside Linkages (5' to 3')" in the table below, wherein each "s" represents a phosphorothioate internucleoside linkage, each "z" represents a mesyl phosphoramidate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 42

5-10-5 MOE gapmers with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	Internucleoside Linkages (5' to 3')	SEQ ID NO
827672	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooooooooooooo	3316
1601249	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooszzzzsssssooss	3316
1601250	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooszzzzsssssooss	3316
1601251	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooszzzzsssssooss	3316
1601257	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooszzzzsssssooss	3318
1601258	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooszzzzsssssooss	3318
1616037	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	ssssssszszssssss	3316
1616038	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	ssssssszszsssssooss	3316
1616039	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	sssoossssssssooss	3319
1616040	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	sssoosssssszsssooss	3319

1616354	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	SSSOSZZSSSSSSSSSS	3320
1616355	22792	22811	24858	24877	GCTCAGTATTCTTTGCATTA	SSOOSZZSSSSSSSOSS	3320
1616357	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSSSS	3318
1616358	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSOSS	3318
1620553	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SOSSSSSSSSSSSOSS	3319
1620554	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SOSSSSSSSSSSSOSS	3319
1620555	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SOSSSSSSSSSSSOSS	3319
1679439	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679440	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679441	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSSSS	3318
1679442	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSOSS	3318
1679443	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSSSS	3318
1679444	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSSSS	3318
1679445	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSSSS	3318
1679446	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SSSSSZSSSSZSSSSSS	3318
1679447	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679448	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679449	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679450	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679451	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679452	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679453	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679454	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SOSSSZSSSSZSSSOSS	3318
1679455	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	SZSSSZSSSSZSSSZSS	3318
1679456	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	ZZSSSZSSSSZSSSSZZ	3318
1679457	17567	17586	19633	19652	ACAGATATTTTGTTCCTGCC	ZSSSZSSSSZSSSSSZ	3318
1679458	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SSOOSZSSSSSZSSSOSS	3319
1679459	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SSSOSZSSSSSZSSSOSS	3319
1679460	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SSOOSZSSSSSZSSSSS	3319
1679461	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SSSSSZSSSSSZSSSOSS	3319
1679462	46675	46694	48741	48760	ACGACATTTTCTTGCTCTT	SSSSZSSSSSZSSSSS	3319
1679463	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SOOOSZSSSSSZSSSOSS	3317
1679464	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SOOOSZSSSSSZSSSOSS	3317
1679465	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSOOSZSSSSSZSSSOSS	3317
1679466	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSOOSZSSSSSZSSSOSS	3317
1679467	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSSOSZSSSSSZSSSOSS	3317
1679468	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSSOSZSSSSSZSSSOSS	3317
1679469	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSSOSZSSSSSZSSSOSS	3317
1679470	22791	22810	24857	24876	CTCAGTATTCTTTGCATTAG	SSSOSZSSSSSZSSSOSS	3317

The modified oligonucleotides in the table below are MOE gapmers containing a 2'- β -D-deoxyxylosyl modification with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): ccccc[bDdx]dddddddeccc; wherein

each “e” represents a 2’-MOE sugar moiety, each “d” represents a 2’-β-D-deoxyribose sugar moiety and each “[bDdx]” represents a 2’-β-D-deoxyxylosyl sugar moiety. The internucleoside linkage motifs for the modified oligonucleotides are presented in the column labeled “Internucleoside Linkages (5’ to 3’)” in the table below, wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 43

MOE gapmers containing a 2’-β-D-deoxyxylosyl modification with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5’ to 3’)	Internucleoside Linkages (5’ to 3’)	SEQ ID NO
1601247	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooooooooooooo	3316
1601255	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooooooooooooo	3318

The modified oligonucleotides in the table below are MOE gapmers containing a 2’-β-D-deoxyxylosyl modification with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeed[bDdx]dddddddeeeeee; wherein each “e” represents a 2’-MOE sugar moiety, each “d” represents a 2’-β-D-deoxyribose sugar moiety and each “[bDdx]” represents a 2’-β-D-deoxyxylosyl sugar moiety. The internucleoside linkage motifs for the modified oligonucleotides are presented in the column labeled “Internucleoside Linkages (5’ to 3’)” in the table below, wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 44

MOE gapmers containing a 2’-β-D-deoxyxylosyl modification with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5’ to 3’)	Internucleoside Linkages (5’ to 3’)	SEQ ID NO
1601248	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooooooooooooo	3316
1601256	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooooooooooooo	3318

The modified oligonucleotides in the table below are MOE gapmers containing a 2’-α-L-deoxyribose modification with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeed[aLdr]dddddddeeeeee; wherein each “e” represents a 2’-MOE sugar moiety, each “d” represents a 2’-β-D-deoxyribose sugar moiety, and each “[aLdr]” represents a 2’-α-L-deoxyribose sugar moiety. The internucleoside linkage motifs for the modified oligonucleotides are presented in the column labeled “Internucleoside Linkages (5’ to 3’)” in the table below, wherein each “s” represents a

phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 45

MOE gapmers containing a 2’-α-L-deoxyribosyl modification with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	Internucleoside Linkages (5' to 3')	SEQ ID NO
1601245	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooooooooooooo	3316
1601253	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooooooooooooo	3318

The modified oligonucleotides in the table below are MOE gapmers containing a 2’-α-L-deoxyribosyl modification with mixed internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeed[aLDr]dddddeeeeee; wherein each “e” represents a 2’-MOE sugar moiety, each “d” represents a 2’-β-D-deoxyribosyl sugar moiety, and each “[aLDr]” represents a 2’-α-L-deoxyribosyl sugar moiety. The internucleoside linkage motifs for the modified oligonucleotides are presented in the column labeled “Internucleoside Linkages (5’ to 3’)” in the table below, wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 46

MOE gapmers containing a 2’-α-L-deoxyribosyl modification with mixed internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	Internucleoside Linkages (5' to 3')	SEQ ID NO
1601246	48854	48873	50920	50939	GTTTTCATCAATATCTGCAA	sooooooooooooo	3316
1601254	17567	17586	19633	19652	ACAGATATTTTGTCTGCC	sooooooooooooo	3318

The modified oligonucleotide in the table below is a MOE gapmer containing cEt modifications with mixed internucleoside linkages. The modified oligonucleotide in the table below are 17 nucleosides in length, wherein the sugar motif for the modified oligonucleotide is (from 5’ to 3’): cckkdddddddkkcc; wherein each “c” represents a 2’-MOE sugar moiety, each “k” represents a cEt sugar moiety, and each “d” represents a 2’-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotide is (from 5’ to 3’): sooozzzzssssoss; wherein each “s” represents a phosphorothioate internucleoside linkage, each “o” represents a phosphodiester internucleoside linkage, and each “z” represents a mesyl phosphoramidate internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 47

MOE gapmer containing cEt modifications with mixed linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	SEQ ID NO
1495436	48854	48870	50920	50936	TTCATCAATATCTGCAA	3332

“Start site” indicates the 5’-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. “Stop site” indicates the 3’-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. The modified oligonucleotides listed in the table below are complementary to SEQ ID NO: 3 (described herein above), or to SEQ ID NO: 4 (Ensembl ID ENST00000618500.4, Ensembl release 106 - Apr 2022). ‘N/A’ indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

The modified oligonucleotides in the table below are 6-10-4 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5’ to 3’): eeeeeedddddddeeee; wherein each “e” represents a 2’-MOE sugar moiety and each “d” represents a 2’-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5’ to 3’): soooooosssssssoss; wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

Table 48

6-10-4 MOE gapmers with mixed PS/PO linkages complementary to human SNCA

Compound No.	SEQ ID No: 3 Start Site	SEQ ID No: 3 Stop Site	SEQ ID No: 4 Start Site	SEQ ID No: 4 Stop Site	Sequence (5' to 3')	SEQ ID NO
1620594	43	62	N/A	N/A	AATTCCTTTACACCACACTC	3333
1620597	N/A	N/A	87	106	TGAATTCCTTTACACCACAT	3334

Example 10: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 2-weeks, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model expressing wildtype full-length *SNCA* gene directed by the human *SNCA* promoter/enhancer regions on the BAC transgene (JAX strain 018442).

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300μg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Two weeks post treatment, mice were sacrificed and RNA was extracted from cortical brain tissue and hippocampus for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (forward sequence TGGCAGAAGCAGCAGGAAA, designated herein as SEQ ID NO: 3339; reverse sequence TCCTTGGTTTGGAGCCTACA, designated herein as SEQ ID NO: 3340; probe sequence CAAAAGAGGGTGTCTC, designated herein as SEQ ID NO: 3341). SNCA RNA levels were normalized to mouse

Ppia. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (forward sequence TCGCCGCTTGCTGCA, designated herein as SEQ ID NO: 3342; reverse sequence ATCGGCCGTGATGTCGA, designated herein as SEQ ID NO: 3343; probe sequence CCATGGTCAACCCCAACCGTGTC, designated herein as SEQ ID NO: 3344). Results are presented as percent human SNCA RNA relative to the amount of human SNCA RNA in PBS treated animals, (% control).

Table 49

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
1484502	6	9
1485336	3	4
1483635	8‡	15‡
1485018	3	4
1483367	30	43
1485638	3	1
1486434	4	7

‡ indicates fewer than 4 samples available

Example 11: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 8-weeks, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Eight weeks post treatment, mice were sacrificed and RNA was extracted from cortical brain tissue and hippocampus for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

Compound 827606 is previously described in WO 2019/164562. Compound 827606 consists of the sequence (from 5' to 3'): ACAGATATTTTGTCTGCC, designated herein as SEQ ID NO: 3318. The sugar motif for Compound No. 827606 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 827606 is (from 5' to 3'): sssssssssssss; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 827606 is a 5-methylcytosine.

Compound 763391 is previously described in WO 2019/164562. Compound 763391 consists of the sequence (from 5' to 3'): GTTTTCATCAATATCTGCAA, designated herein as SEQ ID NO: 3316. The sugar motif for Compound No. 763391 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No.

763391 is (from 5' to 3'): sooooooooooooo; wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 763391 is a 5-methylcytosine.

Compound 827599 is described herein above.

5

Table 50

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300μg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
827606	12	11
1606563	41‡	27‡
1606564	39	38
1606571	37	46
1616037	23	41
1616038	9	19
1616039	4	14
1616357	7	16
1620553	6	9
1620554	3	11
1620555	3	8
1620593	4	11
1620598	9	15
1620603	35	50
1620604	2	8
1620605	6	22

‡ indicates fewer than 4 samples available

10

Table 51

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300μg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
1523524	30	23
1523526	12	14‡
1601249	15	18
1601250	44	28
1601251	16‡	27‡
1601252	37	37
1601257	34	28
1601258	8	7
1601260	25	14
1601261	10	6

1601262	39	38
1601263	38	53
1601264	32	27
1601265	8	9
1601266	16	8
1601267	12	12
1601268	9 [‡]	13 [‡]
1601269	9	12
1601270	14	14
1601271	9	8

[‡] indicates fewer than 4 samples available

Table 52

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
763391	12	21
827599	14 [‡]	7 [‡]
1601245	65 [‡]	88 [‡]
1601246	100	96
1601247	73	91
1601248	42	30
1601253	23	32
1601254	18 [‡]	18 [‡]
1601255	20	15
1601256	28	12

[‡] indicates fewer than 4 samples available

5

Table 53

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
827672	8	10
1535233	24	28
1535317	23	19
1535344	11	9

Table 54

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)
	Cortex
PBS	100

1616040	3
1616358	8
1620596	18

Table 55
Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)
	Cortex
PBS	100
1606566	42
1606568	30
1606572	91
1606573	28
1620589	95
1620591	70
1620594	97
1620595	88‡
1620597	42
1620599	48

‡ indicates fewer than 4 samples available

5

Example 12: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 16-weeks, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

10 The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

 Sixteen weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer
15 probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control). “N.C.” represents datapoints that were not calculated.

 Compound 827714 is previously described in WO 2019/164562. Compound 827714 consists of the sequence (from 5’ to 3’): GTTTTCATCAATATCTGCAA, designated herein as SEQ ID NO: 3316. The sugar motif for Compound No. 827714 is (from 5’ to 3’): eeeeeeeeeeeeeee; wherein each “d” represents a 2’-β-D-deoxyribosyl
20 sugar moiety, and each “e” represents a 2’-MOE sugar moiety. The internucleoside linkage motif for Compound No. 827714 is (from 5’ to 3’): sooooooooooooo; wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 827714 is a 5-methylcytosine.

 Compound 762838 is previously described in WO 2019/164562. Compound 762838 consists of the sequence
25 (from 5’ to 3’): ATGAATTCCTTTACACCACA, designated herein as SEQ ID NO: 3315. The sugar motif for

Compound No. 762838 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 762838 is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 762838 is a 5-methylcytosine.

Compound 763033 is previously described in WO 2019/164562. Compound 763033 consists of the sequence (from 5' to 3'): GCTCAGTATTCTTTGCATTA, designated herein as SEQ ID NO: 3320. The sugar motif for Compound No. 763033 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 763033 is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 763033 is a 5-methylcytosine.

Compound 763032 is previously described in WO 2019/164562. Compound 763032 consists of the sequence (from 5' to 3'): CTCAGTATTCTTTGCATTAG, designated herein as SEQ ID NO: 3317. The sugar motif for Compound No. 763032 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 763032 is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 763032 is a 5-methylcytosine.

Compound 763364, Compound 763391, Compound 827599, Compound 827606, and Compound 789291 are described herein above.

Table 56

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300μg

Compound No.	SNCA RNA (% control)
	Cortex
PBS	100
1616040	6
1616358	12
1620596	24

Table 57

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300μg

Compound No.	SNCA RNA (% control)
PBS	100
763391	75
827599	34
827606	41
827714	38 [‡]
1523524	122

1601245	199
1601246	186
1601247	162
1601248	81
1601249	93
1601250	97
1601251	70
1601252	125
1601253	39
1601254	51
1601255	32
1601256	40 [‡]
1601257	50
1601258	26
1601260	9
1601261	43
1601264	69
1601265	31
1601266	26 [‡]

[‡] indicates fewer than 4 samples available

Table 58

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)
PBS	100
1495436	7
1616037	35
1616038	24
1616039	12
1616357	4
1620605	35

5

Table 59

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)
PBS	100 [‡]
762838	55
763033	65
789291	65
1601262	44
1601267	35
1601269	56
1606566	35

1606572	55‡
1616354	29‡
1616355	15
1620589	78
1620591	61
1620597	59‡
1620599	68
1620633	59
1620635	61

‡ indicates fewer than 4 samples available

Example 13: Duration of Action study of modified oligonucleotides complementary to human SNCA in transgenic mice, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Mice were sacrificed at various timepoints as indicated in the table below and RNA was extracted from cortical brain tissue for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set

hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

Compound 827599 is a comparator compound and is described herein above.

Table 60

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300 µg

Compound No.	Timepoint (Days post-dose)	SNCA RNA (% control)
PBS	28	100‡
	56	100
	84	100
	168	100
	224	100‡
1601258	28	12‡
	56	33
	84	23‡
	168	37
	224	69‡
1601260	28	27‡
	56	3‡
	84	9
	168	27
	224	52

1616357	28	10
	56	9
	84	8‡
	168	30
	224	42‡

‡ indicates fewer than 4 samples available

Table 61

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300 µg

Compound No.	Timepoint (Days post-dose)	SNCA RNA (% control)
PBS	28	100‡
	56	100
	84	100
	168	100
	224	100‡
827599	224	102
1616039	28	4
	56	4‡
	84	5
	168	24
	224	40
1620605	28	9‡
	56	15
	84	45
	168	61
	224	109
1601267	28	8
	56	13
	84	25
	168	71
	224	110

‡ indicates fewer than 4 samples available

5 Example 14: Potency of modified oligonucleotides complementary to human SNCA in transgenic mice, 12-weeks, multiple dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

Treatment

- 10** The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of modified oligonucleotide at doses indicated in the tables below. A group of 4 mice received a single ICV bolus with PBS as a negative control.

RNA analysis

12 weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for quantitative real-time RTPCR analysis of RNA expression of SNCA using human primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

The half maximal effective dose (ED₅₀) of each modified oligonucleotide was calculated using GraphPad Prism 7 software (GraphPad Software, San Diego, CA).

Compound 827599 is a comparator compound and is described herein above.

10

Table 62
Dose-dependent percent reduction of human SNCA mRNA in transgenic mice

Compound No.	Dose (µg)	SNCA % (control)	
		Cortex	ED50 (µg)
PBS	-	100	-
827599	10	104	122
	30	84	
	100	52	
	300	28	
	700	15‡	
1601258	10	73	50
	30	64	
	100	37	
	300	21‡	
	700	6	
1601260	10	65	46
	30	67	
	100	41	
	300	13	
	700	6	

‡ indicates fewer than 4 samples available

Table 63
Dose-dependent percent reduction of human SNCA mRNA in transgenic mice

Compound No.	Dose (µg)	SNCA % (control)	
		Cortex	ED50 (µg)
PBS	-	100	-
1616357	10	79	29
	30	41‡	
	100	28	
	300	6	
	700	4	
1616039	10	70	23
	30	41‡	

	100	17	
	300	14	
	700	4	
1620605	10	100‡	252
	30	107	
	100	83‡	
	300	41	
	700	16‡	

‡ indicates fewer than 4 samples available

Example 15: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 24-weeks, single dose

5 Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

20 Twenty-four weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

15 Compound 763032 is previously described in WO 2019/164562. Compound 763032 consists of the sequence (from 5' to 3'): CTCAGTATTCTTTGCATTAG, designated herein as SEQ ID NO: 3317. The sugar motif for Compound No. 763032 is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. The internucleoside linkage motif for Compound No. 763032 is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage. Each cytosine nucleobase in Compound No. 763032 is a 5-methylcytosine.

Compound 827599 and compound 763364 are described herein above.

Table 64

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300 µg

Compound No.	SNCA RNA (% control)
	Cortex
PBS	100
763032	58
763364	35
827599	98
1616040	10

1679439	21
1679440	47
1679441	16
1679442	24
1679443	38
1679444	16
1679445	14
1679446	8
1679447	35
1679448	42
1679449	27
1679450	27
1679451	31
1679452	32
1679453	45
1679454	29
1679455	22
1679456	11
1679457	17
1679458	41
1679459	12
1679460	22
1679461	41
1679462	16
1679463	90
1679464	149
1679465	63
1679466	78
1679467	59
1679468	87
1679469	65
1679470	36

Example 16: Design of modified oligonucleotides complementary to human SNCA RNA

Modified oligonucleotide complementary to a human SNCA RNA was designed as described in the table below.

“Start site” indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target
5 nucleic acid sequence. “Stop site” indicates the 3'-most nucleoside to which the modified oligonucleotide is
complementary in the target nucleic acid sequence. The modified oligonucleotide listed in the table below is 100%
complementary to SEQ ID NO: 1 (described herein above), or to SEQ ID NO: 2 (described herein above), or to both.

The modified oligonucleotide in the table below is a 5-10-5 MOE gapmer with mixed PS/PO internucleoside
linkages. The modified oligonucleotide is 20 nucleosides in length, wherein the sugar motif for the modified
10 oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein each “e” represents a 2'-MOE sugar moiety and each

“d” represents a 2’-β-D-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotide is presented in the column labeled “Internucleoside Linkages (5’ to 3’)” in the table below, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

5

Table 65

5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages complementary to human SNCA

Compound No.	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	Sequence (5' to 3')	Internucleoside Linkages (5' to 3')	SEQ ID NO
827615	26388	26407	28454	28473	GACTGTAATCTAGGACCCAG	sossssssssssooss	3345

Example 17: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 2-weeks, single dose

10 Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300μg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

15 Two weeks post treatment, mice were sacrificed and RNA was extracted from cortical brain tissue and hippocampus for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of human SNCA RNA in PBS treated animals, (% control).

Compound 827599 is described herein above.

20

Table 66

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300μg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
827615	27	14

Example 18: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 8-weeks, single dose

25 Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300μg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Eight weeks post treatment, mice were sacrificed and RNA was extracted from cortical brain tissue and hippocampus for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

Compound 827599 is described herein above.

Table 67

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA RNA (% control)	
	Cortex	Hippocampus
PBS	100	100
827599	10	9
827615	54	25

Example 19: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 2-weeks, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Two weeks post treatment, mice were sacrificed and RNA was extracted from cortical brain tissue and hippocampus for real-time PCR analysis of measurement of mRNA expression of SNCA using primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of human SNCA RNA in PBS treated animals, (% control).

Table 68

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300µg

Compound No.	SNCA (% control)
PBS	100
827599	21
1616039	6
1601260	30
1620605	54
1616357	45

Example 20: Activity of modified oligonucleotides complementary to human SNCA in transgenic mice, 2-weeks, single dose

Modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)^{Mjfa} transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 2-4 mice each. Each mouse received a single ICV bolus of 300µg of modified oligonucleotide. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Two weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for quantitative real-time RT-PCR analysis of RNA expression of SNCA using human primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control). Each experiment is identified in separate tables below.

Table 69

Reduction of human SNCA mRNA in transgenic mice

Compound No.	SNCA (% control)
PBS	100
827599	19

Table 70

Reduction of human SNCA mRNA in transgenic mice

Compound No.	SNCA (% control)
PBS	100
1616357	12

Example 21: Duration of Action study of a modified oligonucleotide complementary to human SNCA in transgenic mice

FIG. 1 illustrates the duration of action in the CNS of an exemplary modified oligonucleotide disclosed above comprising mesyl phosphoramidate internucleoside linkage compared to a modified oligonucleotide without the mesyl phosphoramidate internucleoside linkage modification. In particular, FIG. 1 illustrates the duration of action for Compound Nos. 1616357 (labeled as MsPA ASO) and 827599 (labeled as ASO). The duration of action study was carried out to 32 weeks post injection. As shown by FIG. 1, Compound No. 1616357 maintained a higher percentage of SNCA mRNA inhibition (i.e., a lower percentage of SNCA mRNA) up to 32 weeks compared to Compound No. 827599. The column labeled “Table” in the table below indicates the source for each datapoint taken from the examples herein above. If multiple experiments were used, the average of the values is presented in the table below. MsPA ASO: antisense oligonucleotide (ASO) with mesyl phosphoramidate internucleoside linkage (MsPA) modification.

Table 71

Reduction of human SNCA RNA in SNCA transgenic mice at a dose of 300 µg

Compound No.	Time point (weeks post ICV)	SNCA RNA (% control)	Table
827599	2	19	69
	8	10	67
	12	28	62
	16	34	57
	24	98	64
	32	102	61
1616357	2	12	70
	4	10	60
	8	8	50; 60
	12	7	60; 63
	16	4	58
	24	30	60
	32	42	60

- 5 FIG. 2 illustrates the concentration of Compound No. 1616357 (labeled as MsPA ASO) in the cortex compared to Compound No. 827599 (labeled as ASO). Compound concentration in tissue is expressed in µg/g. The specific compound concentrations are listed in Table 72.

Table 72

Concentration of modified oligonucleotide in Cortex in SNCA transgenic mice at a dose of 300 µg

Compound No.	Time point (Days post ICV)	Compound Concentration (µg/g)	T 1/2 (Days)
827599	14	13.57	45.4
	84	2.27	
	112	1.48	
	244	0.37	
1616357	14	29.10	115.1
	28	16.90	
	56	18.95	
	84	16.13	
	112	16.92	
	168	7.96	
	244	7.20	

FIG. 3 illustrates the concentration of an exemplary modified oligonucleotide disclosed above comprising mesyl phosphoramidate internucleoside linkage (labeled as MsPA ASO) in the cortex compared to a modified oligonucleotide without the mesyl phosphoramidate internucleoside linkage modification (labeled as ASO).

Example 22: Potency of modified oligonucleotides complementary to human SNCA RNA in human SNCA transgenic mice, 12-weeks

The modified oligonucleotides described above were tested in the FVB/N-Tg(SNCA)Mjfa transgenic mouse model described herein above.

The SNCA transgenic mice were divided into groups of 4 mice each. Each mouse received a single ICV bolus of modified oligonucleotide at various doses indicated in the table below. A group of 4 mice received a single ICV bolus of PBS as a negative control.

Twelve weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for RT-PCR analysis to measure amount of SNCA RNA using human primer probe set hSNCA_LTS00672_MGB (described herein above). SNCA RNA levels were normalized to mouse *Ppia*. Mouse *Ppia* was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human SNCA RNA relative to the amount of SNCA RNA in PBS treated animals, (% control).

The half maximal effective dose (ED₅₀) of each modified oligonucleotide was calculated using GraphPad Prism 10 software (GraphPad Software, San Diego, CA).

Table 73
Dose-dependent reduction of human SNCA mRNA in human SNCA transgenic mice

Compound No.	Dose (µg)	SNCA (% control)	
		Cortex	ED ₅₀ (µg)
PBS	0	100	-
763364	10	116	63
	30	87	
	100	22	
	300	5	
	700	3	

WHAT IS CLAIMED:

1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of a SNCA nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar and a modified internucleoside linkage.
2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 13-3334, wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.
3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases complementary to:
 - an equal length portion of nucleobases 16,692-16,716 of SEQ ID NO: 1 or nucleobases 18,758-18,782 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 18,568-18,593 of SEQ ID NO: 1 or nucleobases 20,634-20,659 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 18,621-18,649 of SEQ ID NO: 1 or nucleobases 20,687-20,715 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 18,721-18,752 of SEQ ID NO: 1 or nucleobases 20,787-20,818 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 19,423-19,443 of SEQ ID NO: 1 or nucleobases 21,489-21,509 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 19,555-19,575 of SEQ ID NO: 1 or nucleobases 21,621-21,641 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 21,457-21,501 of SEQ ID NO: 1 or nucleobases 23,523-23,567 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 22,008-22,030 of SEQ ID NO: 1 or nucleobases 24,074-24,096 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 22,507-22,529 of SEQ ID NO: 1 or nucleobases 24,573-24,595 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 22,614-22,637 of SEQ ID NO: 1 or nucleobases 24,680-24,703 of SEQ ID NO: 2;
 - an equal length portion of nucleobases 25,049-25,090 of SEQ ID NO: 1 or nucleobases 27,115-27,156 of SEQ ID NO: 2;

an equal length portion of nucleobases 26,367-26,388 of SEQ ID NO: 1 or nucleobases 28,433-28,454 of SEQ ID NO: 2;

an equal length portion of nucleobases 26,508-26,531 of SEQ ID NO: 1 or nucleobases 28,574-28,597 of SEQ ID NO: 2;

an equal length portion of nucleobases 30,207-30,226 of SEQ ID NO: 1 or nucleobases 32,273-32,292 of SEQ ID NO: 2;

an equal length portion of nucleobases 31,412-31,438 of SEQ ID NO: 1 or nucleobases 33,478-33,504 of SEQ ID NO: 2;

an equal length portion of nucleobases 33,027-33,057 of SEQ ID NO: 1 or nucleobases 35,093-35,123 of SEQ ID NO: 2; or

an equal length portion of nucleobases 48,460-48,489 of SEQ ID NO: 1 or nucleobases 50,526-50,555 of SEQ ID NO: 2;

wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of:

SEQ ID NO: 78, 2564, 2697, 2747, 2789, 2936, 3063, 3081, 3142, 3189, or 3271;

SEQ ID NO: 206, 231, 270, 316, 2486, 2558, 3041, 3076, 3137, 3184, or 3266;

SEQ ID NO: 64, 128, 289, 921, 2744, 2853, 2922, 3031, 3057, 3099, 3123, 3132, 3160, 3207, 3231, 3289, or 3313;

SEQ ID NO: 227, 427, 545, 1214, 1279, 1385, 1401, 1476, 1616, 3048, 3115, 3176, or 3305;

SEQ ID NO: 203, 285, 1974, 2044, 2949, 3021, 3090, 3151, 3198, or 3280;

SEQ ID NO: 205, 2594, 2686, 3028, 3097, 3158, 3205, or 3287;

SEQ ID NO: 214, 247, 865, 1887, 1948, 3067, 3085, 3146, 3193, or 3275;

SEQ ID NO: 167, 208, 248, 304, 1930, 3054, 3120, 3129, 3228, or 3310;

SEQ ID NO: 196, 1814, 1909, 3042, 3109, 3170, 3217, or 3299;

SEQ ID NO: 171, 207, 245, 489, 2390, 3053, 3119, 3128, 3227, or 3309;

SEQ ID NO: 24, 133, 199, 228, 230, 276, 314, 946, 2759, 2818, 2873, 3069, 3087, 3148, 3195, or 3277;

SEQ ID NO: 168, 193, 236, 313, 2446, 3049, 3116, 3177, 3224, or 3306;

SEQ ID NO: 210, 223, 272, 273, 274, 1026, 1143, 3020, 3089, 3150, 3197, or 3279;

SEQ ID NO: 287, 964, 1040, 1154, 3050, 3117, 3178, 3225, or 3307;

SEQ ID NO: 119, 980, 1085, 1166, 3051, 3118, 3127, 3226, or 3308;

SEQ ID NO: 194, 277, 1113, 1185, 1309, 3024, 3093, 3154, 3201, or 3283; or

SEQ ID NO: 310, 803, 919, 1582, 1674, 3032, 3032, 3032, 3100, 3161, 3208, 3290, or 3290;

wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

5. The oligomeric compound of any of claims 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 85%, at least 90%, at least 95%, or 100% complementary to the nucleobase sequence of any one of SEQ ID NOs: 1-9 when measured across the entire nucleobase sequence of the modified oligonucleotide.
6. The oligomeric compound of any of claims 1-5, wherein the modified oligonucleotide consists of 12 to 20, 12 to 25, 12 to 30, 12 to 50, 13 to 20, 13 to 25, 13 to 30, 13 to 50, 14 to 20, 14 to 25, 14 to 30, 14 to 50, 15 to 20, 15 to 25, 15 to 30, 15 to 50, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 16 to 50, 17 to 20, 17 to 25, 17 to 30, 17 to 50, 18 to 20, 18 to 25, 18 to 30, 18 to 50, 19 to 20, 19 to 25, 19 to 30, 19 to 50, 20 to 25, 20 to 30, or 20 to 50 linked nucleosides.
7. The oligomeric compound of any of claims 1-6, wherein at least one nucleoside of the modified oligonucleotide is a modified nucleoside.
8. The oligomeric compound of claim 7, wherein the modified nucleoside comprises a modified sugar moiety.
9. The oligomeric compound of claim 8, wherein the modified sugar moiety comprises a bicyclic sugar moiety.
10. The oligomeric compound of claim 9, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂-, and -O-CH(CH₃)-,
11. The oligomeric compound of any of claims 7-10, wherein the modified nucleoside comprises a non-bicyclic modified sugar moiety.
12. The oligomeric compound of claim 11, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, a 2'-β-D-deoxyxylosyl sugar moiety, or a 2'-α-L-deoxyribosyl sugar moiety.
13. The oligomeric compound of any of claims 7-12, wherein the modified nucleoside comprises a sugar surrogate.
14. The oligomeric compound of claim 13, wherein the sugar surrogate is any of morpholino, modified morpholino, glycol nucleic acid (GNA), six-membered tetrahydropyran (THP), and F-hexitol nucleic acid (F-HNA).
15. The oligomeric compound of any of claims 1-14, wherein the modified oligonucleotide is a gapmer.
16. The oligomeric compound of any of claims 1-15, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.
17. The oligomeric compound of claim 16, wherein at least one internucleoside linkage is a phosphodiester internucleoside linkage.
18. The oligomeric compound of claim 16 or claim 17, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.
19. The oligomeric compound of any of claims 16-18, wherein at least one modified internucleoside linkage is a mesyl phosphoramidate internucleoside linkage.
20. The oligomeric compound of any of claims 16-19, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, and a mesyl phosphoramidate internucleoside linkage.
21. The oligomeric compound of any of claims 16, 18, or 19, wherein each internucleoside linkage is independently selected from a phosphorothioate internucleoside linkage and a mesyl phosphoramidate internucleoside linkage.
22. The oligomeric compound of any of claims 16-18, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.

23. The oligomeric compound of any of claims 16-22, wherein at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, or 19 internucleoside linkages of the modified oligonucleotide are phosphorothioate internucleoside linkages.

24. The oligomeric compound of any of claims 16-21, wherein at least 1, at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, or at least 8 internucleoside linkages of the modified oligonucleotide are mesyl phosphoramidate internucleoside linkages.

[illegible]

26. The oligomeric compound of any of claims 1-25, wherein at least one nucleoside of the modified oligonucleotide comprises a modified nucleobase.

27. The oligomeric compound of claim 26, wherein the modified nucleobase is a 5-methylcytosine.

28. The oligomeric compound of claim 27, wherein each cytosine is a 5-methylcytosine.

29. The oligomeric compound of any of claims 1-28, wherein each nucleoside of the modified oligonucleotide is unmodified adenine, unmodified guanine, unmodified thymine, unmodified cytosine, or 5-methylcytosine.

30. The oligomeric compound of any of claims 1-29, wherein the modified oligonucleotide comprises a deoxy region.

31. The oligomeric compound of claim 30, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.

32. The oligomeric compound of claim 30 or claim 31, wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.

33. The oligomeric compound of any of claims 30-32, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.

34. The oligomeric compound of any of claims 30-33, wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein at least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety.
35. The oligomeric compound of claim 34, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.
36. The oligomeric compound of claim 34 or claim 35, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.
37. The oligomeric compound of any of claims 1-36, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22 or 18-20 linked nucleosides.
38. The oligomeric compound of any of claims 1-37, wherein the modified oligonucleotide consists of 20 linked nucleosides.
39. The oligomeric compound of any of claims 1-38, wherein the modified oligonucleotide comprises:
a 5'-region consisting of 1-6 linked 5'-region nucleosides;
a central region consisting of 6-10 linked central region nucleosides; and
a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.
40. The oligomeric compound of any of claims 1-39, wherein the modified oligonucleotide has a sugar motif comprising:
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.
41. The oligomeric compound of claim 40, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.
42. The oligomeric compound of any of claims 1-39, wherein the modified oligonucleotide has a sugar motif comprising:
a 5'-region consisting of 6 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 4 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety and each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.
43. The oligomeric compound of claim 42, wherein the modified oligonucleotide has

a 5'-region consisting of 6 linked 5'-region nucleosides;
 a central region consisting of 10 linked central region nucleosides; and
 a 3'-region consisting of 4 linked 3'-region nucleosides; wherein
 each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety and
 each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.

44. The oligomeric compound of any of claims 1-43, consisting of the modified oligonucleotide.
45. The oligomeric compound of any of claims 1-43, wherein the oligomeric compound comprises a conjugate group.
46. The oligomeric compound of claim 45, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.
47. The oligomeric compound of claim 46, wherein the conjugate linker is a phosphodiester linker.
48. The oligomeric compound of claim 46, wherein the conjugate linker consists of a single bond.
49. The oligomeric compound of any of claims 46 - 48, wherein the conjugate linker is cleavable.
50. The oligomeric compound of any of claims 46, 47, or 49, wherein the conjugate linker comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the modified oligonucleotide, or to another linker-nucleoside by a phosphodiester bond.
51. The oligomeric compound of any of claims 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.
52. The oligomeric compound of any of claims 45-50, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.
53. The oligomeric compound of any of claims 1-49 or 51-52, wherein the oligomeric compound does not comprise linker-nucleosides.
54. The oligomeric compound of any of claims 1-53, comprising a terminal group.
55. The oligomeric compound of claim 54, wherein the terminal group is an abasic sugar moiety.
56. The oligomeric compound of any of claims 1-55, wherein the oligomeric compound is an RNase H agent.
57. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$A_{es}^m C_{es} A_{es} G_{es} A_{es} T_{dz} A_{dz} T_{dz} T_{dz} T_{ds} T_{ds} G_{ds} T_{ds} T_{ds}^m C_{es} T_{es} G_{es}^m C_{es}^m C_e$ (SEQ ID NO: 3335), wherein:

A = an adenine nucleobase,
 mC = a 5-methylcytosine nucleobase,
 G = a guanine nucleobase,
 T = a thymine nucleobase,
 e = a 2'-MOE sugar moiety,
 d = a 2'-β-D-deoxyribose sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

58. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$A_{es}^m C_{es} G_{eo} A_{eo}^m C_{es} A_{dz} T_{ds} T_{ds} T_{ds}^m C_{ds} T_{ds} T_{dz} G_{ds}^m C_{ds}^m C_{es} T_{eo}^m C_{es} T_{es} T_e$ (SEQ ID NO: 3336), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage,

z = a mesyl phosphoramidate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

59. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$A_{es}{}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{ds}T_{ds}T_{ds}T_{dz}G_{dz}T_{ds}T_{ds}{}^mC_{es}T_{es}G_{es}{}^mC_{es}{}^mC_e$ (SEQ ID NO: 3337), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

60. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation:

$A_{es}T_{eo}{}^mC_{eo}A_{eo}{}^mC_{eo}G_{eo}A_{ds}{}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}{}^mC_{ds}T_{ds}T_{ds}G_{eo}{}^mC_{es}{}^mC_{es}T_e$ (SEQ ID NO: 3338), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group or a terminal group.

61. The oligomeric compound of any of claims 57-60, wherein the modified oligonucleotide is a pharmaceutically acceptable salt.

62. The oligomeric compound of claim 61, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

63. The oligomeric compound of any of claims 1-62, wherein the oligomeric compound is a singled-stranded oligomeric compound.

64. An oligomeric compound according to the following chemical notation:

$N^1_{es}{}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{dz}T_{ds}T_{ds}T_{ds}G_{ds}T_{ds}T_{ds}{}^mC_{es}T_{es}G_{es}{}^mC_{es}N^2_e$ (SEQ ID NO: 3346), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,

N² = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein when N² is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

65. An oligomeric compound according to the following chemical notation:

N¹_{es}^mC_{es}G_{eo}A_{eo}^mC_{es}A_{dz}T_{ds}T_{ds}T_{ds}^mC_{ds}T_{ds}T_{dz}G_{ds}^mC_{ds}^mC_{es}T_{eo}^mC_{es}T_{es}N³_e (SEQ ID NO: 3347), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,

N³ = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N³ is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage,

z = a mesyl phosphoramidate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

66. An oligomeric compound according to the following chemical notation:

N¹_{es}^mC_{es}A_{es}G_{es}A_{es}T_{dz}A_{dz}T_{ds}T_{ds}T_{ds}T_{dz}G_{dz}T_{ds}T_{ds}^mC_{es}T_{es}G_{es}^mC_{es}N²_e (SEQ ID NO: 3348), wherein:

A = an adenine nucleobase,

^mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

N¹ = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N¹ is absent its sugar and internucleoside linkage are also absent,

N² = a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent, wherein when N² is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,
 d = a 2'-β-D-deoxyribosyl sugar moiety,
 s = a phosphorothioate internucleoside linkage, and
 z = a mesyl phosphoramidate internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

67. An oligomeric compound according to the following chemical notation:

$N^1_{es}T_{eo}{}^mC_{eo}A_{eo}{}^mC_{eo}G_{eo}A_{ds}{}^mC_{ds}A_{ds}T_{ds}T_{ds}T_{ds}{}^mC_{ds}T_{ds}T_{ds}G_{eo}{}^mC_{es}{}^mC_{es}N^3_e$ (SEQ ID NO: 3349), wherein:

A = an adenine nucleobase,

mC = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

N^1 = an adenine nucleobase, a modified adenine, a hypoxanthine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^1 is absent its sugar and internucleoside linkage are also absent,

N^3 = a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent, wherein when N^3 is absent its sugar is also absent,

e = a 2'-MOE sugar moiety,

d = a 2'-β-D-deoxyribosyl sugar moiety,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage; and

wherein the oligomeric compound optionally comprises a conjugate group.

68. The oligomeric compound of any of claims 64-67, wherein N^1 is an adenine nucleobase.

69. The oligomeric compound of any of claims 64-67, wherein N^1 is an unmodified adenine.

70. The oligomeric compound of any of claims 64-67, wherein N^1 is a modified adenine.

71. The oligomeric compound of any of claims 64-67, wherein N^1 is a hypoxanthine.

72. The oligomeric compound of any of claims 64-67, wherein N^1 is an abasic sugar moiety.

73. The oligomeric compound of any of claims 64-67, wherein N^1 is a terminal group.

74. The oligomeric compound of any of claims 64-67, wherein N^1 is absent.

75. The oligomeric compound of any of claims 64-74, wherein N^2 is a modified cytosine.

76. The oligomeric compound of any of claims 64-74, wherein N^2 is 5-methylcytosine.

77. The oligomeric compound of any of claims 64-74, wherein N^2 is an unmodified cytosine.

78. The oligomeric compound of any of claims 64-74, wherein N^2 is an abasic sugar moiety.

79. The oligomeric compound of any of claims 64-74, wherein N^2 is a terminal group.

80. The oligomeric compound of any of claims 64-74, wherein N^2 is absent.

81. The oligomeric compound of any of claims 64-74, wherein N^3 is a modified thymine.

82. The oligomeric compound of any of claims 64-74, wherein N^3 is an unmodified thymine.

83. The oligomeric compound of any of claims 64-74, wherein N^3 is an abasic sugar moiety.

84. The oligomeric compound of any of claims 64-74, wherein N^3 is a terminal group.

85. The oligomeric compound of any of claims 64-74, wherein N^3 is absent.

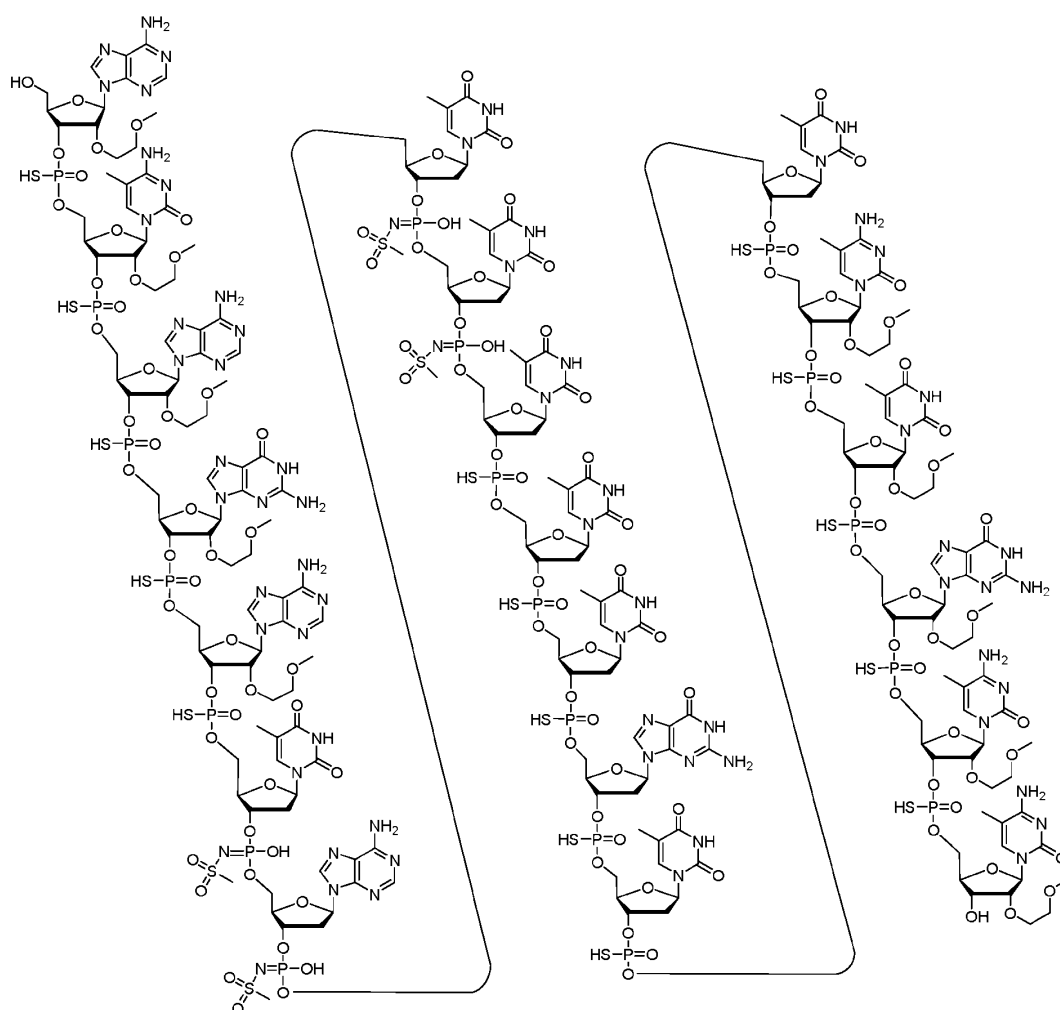
86. The oligomeric compound of any of claims 64-80, wherein N¹ is an adenine nucleobase and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
87. The oligomeric compound of any of claims 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is a modified cytosine.
88. The oligomeric compound of any of claims 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is an abasic sugar moiety.
89. The oligomeric compound of any of claims 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is a terminal group.
90. The oligomeric compound of any of claims 64-80 or 86, wherein N¹ is an adenine nucleobase and N² is absent.
91. The oligomeric compound of any of claims 64-80, wherein N¹ is a modified adenine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
92. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a modified adenine and N² is a modified cytosine.
93. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a modified adenine and N² is 5-methylcytosine.
94. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a modified adenine and N² is an abasic sugar moiety.
95. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a modified adenine and N² is a terminal group.
96. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a modified adenine and N² is absent.
97. The oligomeric compound of any of claims 64-80 or 91, wherein N¹ is a hypoxanthine and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
98. The oligomeric compound of any of claims 64-80 or 97, wherein N¹ is a hypoxanthine and N² is a modified cytosine.
99. The oligomeric compound of any of claims 64-80 or 97, wherein N¹ is a hypoxanthine and N² is 5-methylcytosine.
100. The oligomeric compound of any of claims 64-80 or 97, wherein N¹ is a hypoxanthine and N² is an abasic sugar moiety.
101. The oligomeric compound of any of claims 64-80 or 97, wherein N¹ is a hypoxanthine and N² is a terminal group.
102. The oligomeric compound of any of claims 64-80 or 97, wherein N¹ is a hypoxanthine and N² is absent.
103. The oligomeric compound of any of claims 64-80, wherein N¹ is an abasic sugar moiety and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
104. The oligomeric compound of any of claims 64-80, wherein N¹ is a terminal group and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
105. The oligomeric compound of any of claims 64-80, wherein N¹ is absent and N² is a cytosine nucleobase, a modified cytosine, an abasic sugar moiety, a terminal group, or is absent.
106. The oligomeric compound of any of claims 64-80, wherein N¹ is absent and N² is absent.

107. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is an adenine nucleobase and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
108. The oligomeric compound of any of claims 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a thymine nucleobase.
109. The oligomeric compound of any of claims 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a modified thymine.
110. The oligomeric compound of any of claims 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is an abasic sugar moiety.
111. The oligomeric compound of any of claims 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is a terminal group.
112. The oligomeric compound of any of claims 64-74, 81-85, or 107, wherein N¹ is an adenine nucleobase and N³ is absent.
113. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is a modified adenine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
114. The oligomeric compound of any of claims 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is an unmodified thymine.
115. The oligomeric compound of any of claims 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is an abasic sugar moiety.
116. The oligomeric compound of any of claims 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is a terminal group.
117. The oligomeric compound of any of claims 64-74, 81-85, or 113, wherein N¹ is a modified adenine and N³ is absent.
118. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is a hypoxanthine and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
119. The oligomeric compound of any of claims 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is an unmodified thymine.
120. The oligomeric compound of any of claims 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is an abasic sugar moiety.
121. The oligomeric compound of any of claims 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is a terminal group.
122. The oligomeric compound of any of claims 64-74, 81-85, or 118, wherein N¹ is a hypoxanthine and N³ is absent.
123. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is an abasic sugar moiety and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
124. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is a terminal group and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
125. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is absent and N³ is a thymine nucleobase, a modified thymine, an abasic sugar moiety, a terminal group, or is absent.
126. The oligomeric compound of any of claims 64-74 or 81-85, wherein N¹ is absent and N³ is absent.

127. The oligomeric compound of any of claims 64-126, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.
128. The oligomeric compound of claim 127, wherein the conjugate linker is a phosphodiester linker.
129. The oligomeric compound of claim 127, wherein the conjugate linker consists of a single bond.
130. The oligomeric compound of any of claims 127-129, wherein the conjugate linker is cleavable.
131. The oligomeric compound of any of claims 127, 128, or 130, wherein the conjugate linker comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the oligomeric compound, or to another linker-nucleoside by a phosphodiester bond.
132. The oligomeric compound of any of claims 64-131, wherein the conjugate group is attached to the oligomeric compound at the 5'-end of the oligomeric compound.
133. The oligomeric compound of any of claims 64-131, wherein the conjugate group is attached to the oligomeric compound at the 3'-end of the oligomeric compound.
134. The oligomeric compound of any of claims 64-133, wherein the oligomeric compound is a pharmaceutically acceptable salt.
135. The oligomeric compound of claim 133, wherein the pharmaceutically acceptable salt comprises one or more cations selected from sodium, potassium, calcium, and magnesium.
136. An oligomeric duplex, comprising a first oligomeric compound and a second oligomeric compound comprising a second modified oligonucleotide, wherein the first oligomeric compound is an oligomeric compound of any of claims 1-135.
137. The oligomeric duplex of claim 136, wherein the second modified oligonucleotide consists of 12 to 50 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 8 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.
138. The oligomeric duplex of claim 136 or claim 137, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.
139. The oligomeric duplex of claim 138, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.
140. The oligomeric duplex of any of claims 136-139, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.
141. The oligomeric duplex of claim 140, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.
142. The oligomeric duplex of claim 141, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from $-O-CH_2-$; and $-O-CH(CH_3)-$.
143. The oligomeric duplex of claim 140, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.
144. The oligomeric duplex of claim 143, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-F modified sugar moiety, or 2'-OMe modified sugar moiety.
145. The oligomeric duplex of any of claims 136-144, wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage.

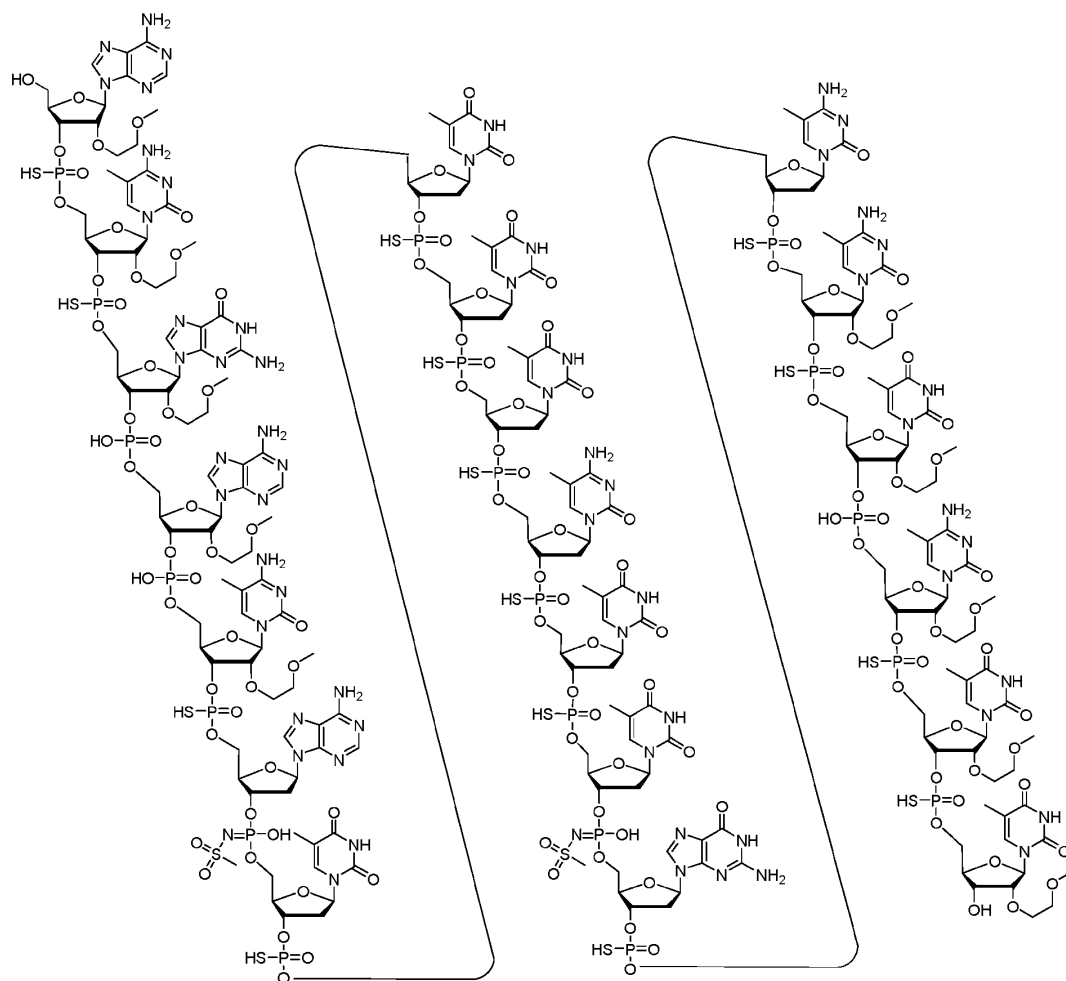
146. The oligomeric duplex of claim 145, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.
147. The oligomeric duplex of any of claims 136-146, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage.
148. The oligomeric duplex of any of claims 145-147, wherein at least one internucleoside linkage of the second modified oligonucleotide is a mesyl phosphoramidate internucleoside linkage.
149. The oligomeric duplex of any of claims 136-148, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, or a mesyl phosphoramidate internucleoside linkage.
150. The oligomeric duplex of any of claims 136-149, wherein the second modified oligonucleotide comprises at least one modified nucleobase.
151. The oligomeric duplex of claim 150, wherein the at least one modified nucleobase of the second modified oligonucleotide is 5-methylcytosine.
152. The oligomeric duplex of any of claims 136-151, wherein the second modified oligonucleotide comprises a conjugate group.
153. The oligomeric duplex of claim 152, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.
154. The oligomeric duplex of claim 153, wherein the conjugate linker consists of a single bond.
155. The oligomeric duplex of claim 153 or claim 154, wherein the conjugate linker is cleavable.
156. The oligomeric duplex of claim 153 or claim 155, wherein the conjugate linker comprises 1-3 linker-nucleosides, wherein at least one linker nucleoside is linked to the conjugate moiety, to the modified oligonucleotide, or to another linker-nucleoside by a phosphodiester bond.
157. The oligomeric duplex of any of claims 153-156, wherein the conjugate linker is a phosphodiester linker.
158. The oligomeric duplex of any of claims 152-157, wherein the conjugate group is attached to the 5'-end of the second modified oligonucleotide.
159. The oligomeric duplex of any of claims 152-157, wherein the conjugate group is attached to the 3'-end of the second modified oligonucleotide.
160. The oligomeric duplex of any of claims 152-157, wherein the conjugate group is attached via the 2' position of a ribosyl sugar moiety at an internal position of the second modified oligonucleotide.
161. The oligomeric duplex of any of claims 152-160, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.
162. The oligomeric duplex of any of claims 152-161, wherein the conjugate group comprises a cell-targeting moiety.
163. The oligomeric duplex of any of claims 136-162, wherein the second modified oligonucleotide comprises a terminal group.
164. The oligomeric duplex of claim 163, wherein the terminal group is an abasic sugar moiety.

165. An antisense agent comprising or consisting of an antisense compound, wherein the antisense compound is the oligomeric compound of any of claims 1-135.
166. An antisense agent, wherein the antisense agent is the oligomeric duplex of any of claims 136-164.
167. The antisense agent of claim 165 or claim 166, wherein the antisense agent is:
- i) an RNase H agent capable of reducing the amount of SNCA nucleic acid through the activation of RNase H; or
 - ii) an RNAi agent capable of reducing the amount of SNCA nucleic acid through the activation of RISC/Ago2.
168. The antisense agent of any of claims 165-167, wherein the antisense agent comprises a conjugate group, and wherein the conjugate group comprises a cell-targeting moiety.
169. A modified oligonucleotide according to the following chemical structure:



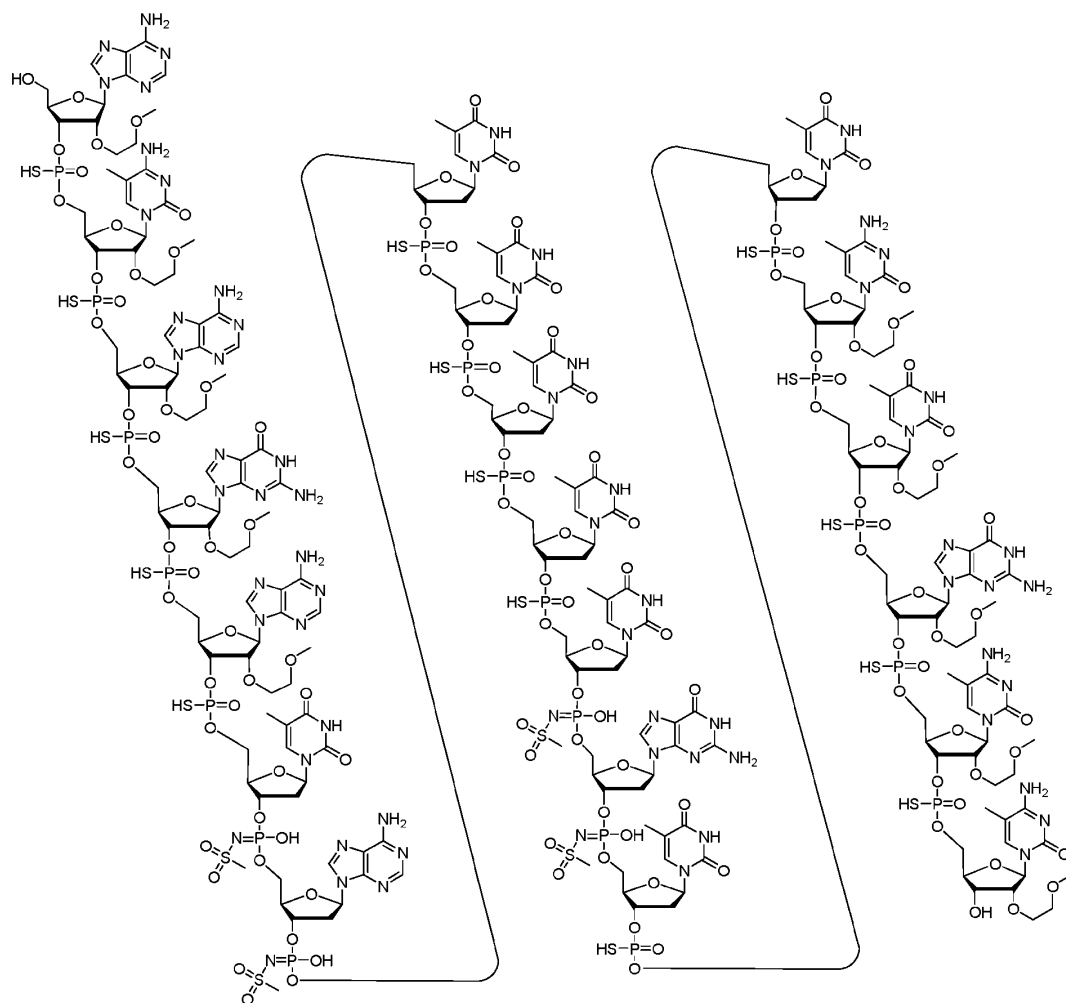
(SEQ ID NO: 3335), or a pharmaceutically acceptable salt thereof.

170. A modified oligonucleotide according to the following chemical structure:

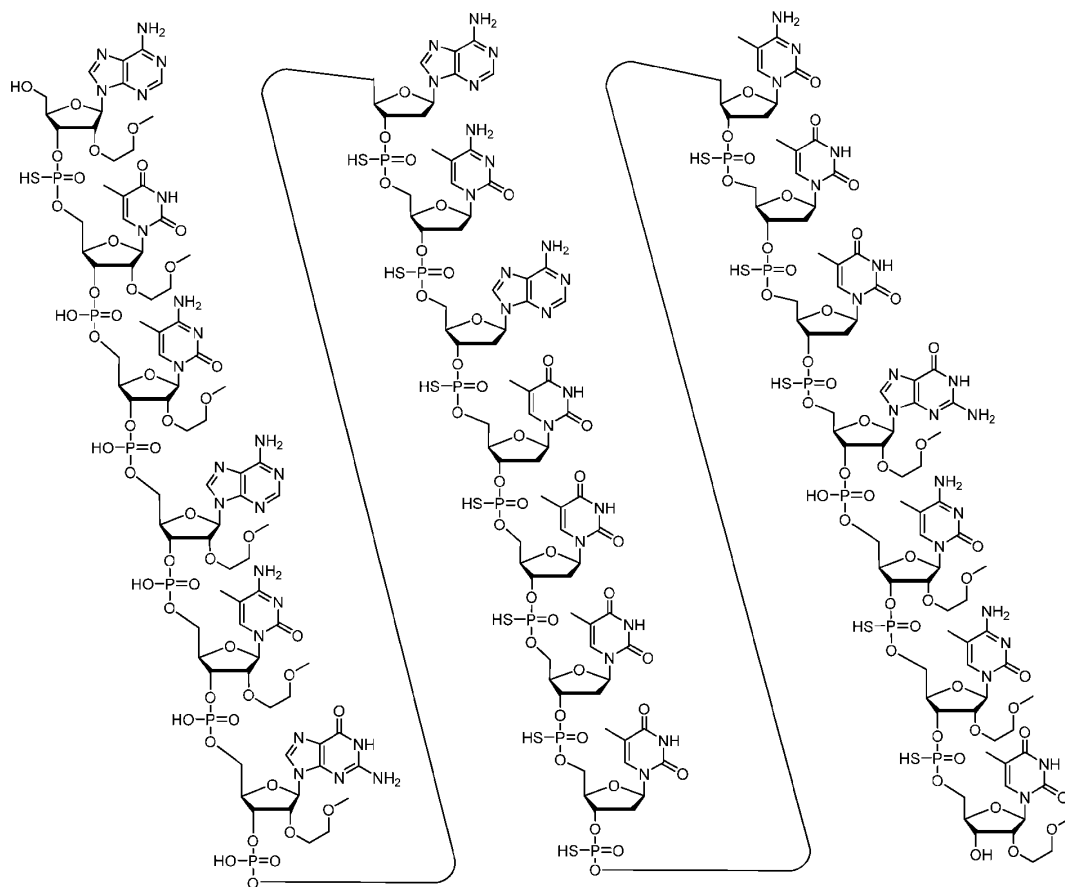


(SEQ ID NO: 3336), or a pharmaceutically acceptable salt thereof.

171. A modified oligonucleotide according to the following chemical structure:



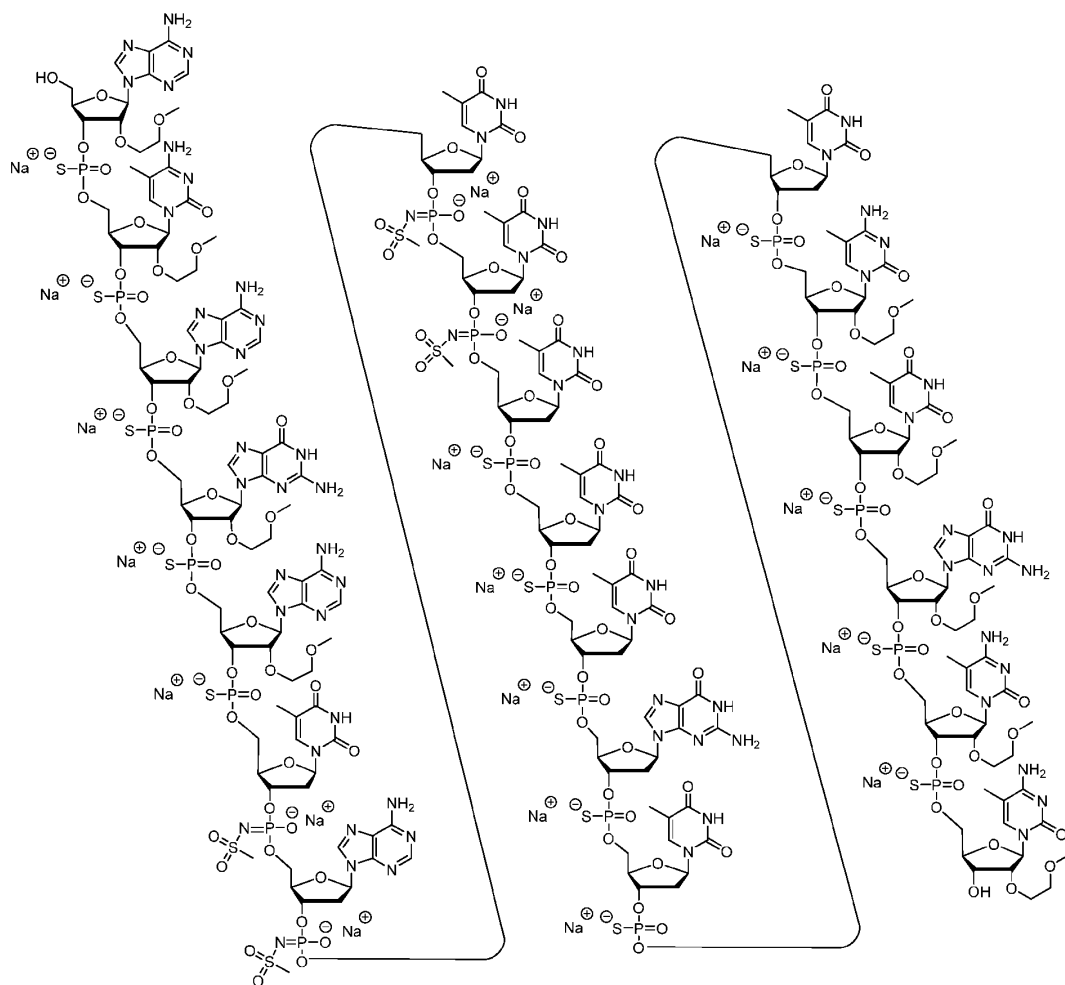
172. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3338), or a pharmaceutically acceptable salt thereof.

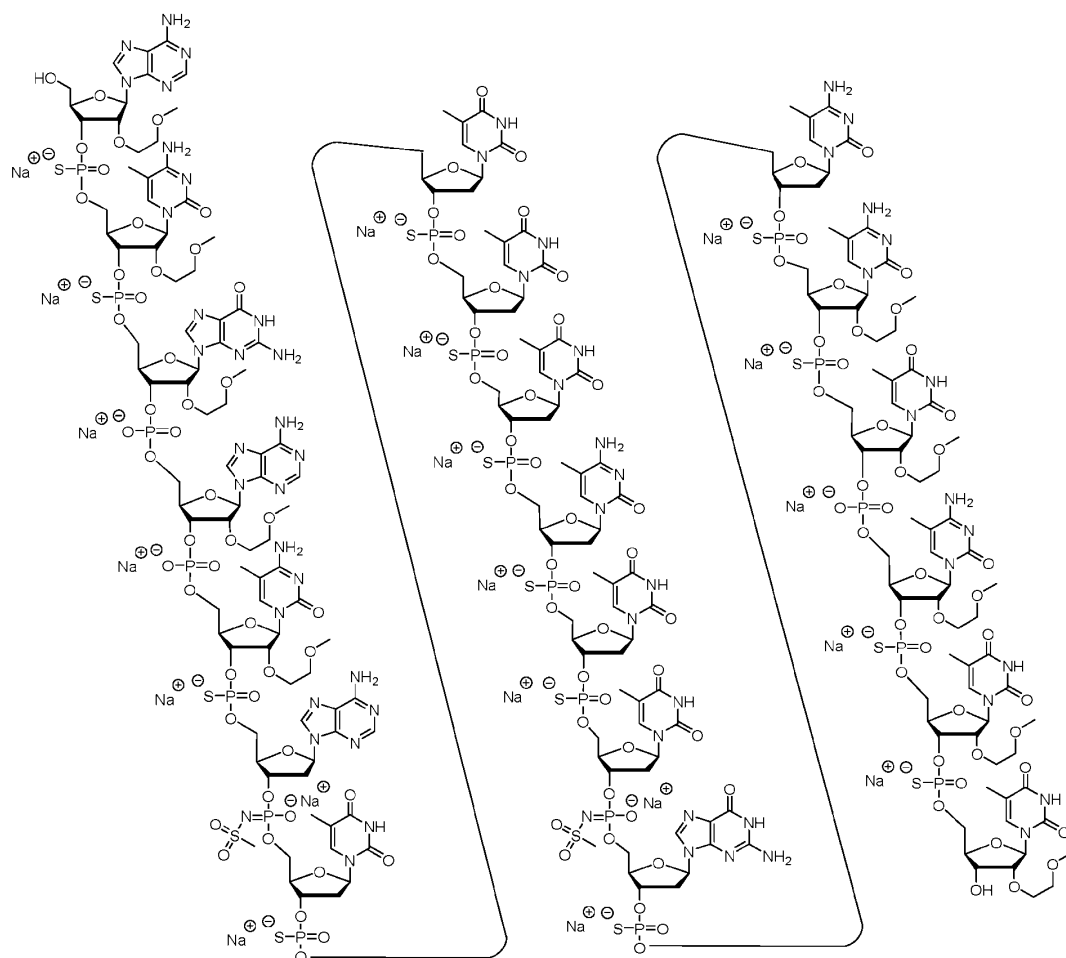
173. The modified oligonucleotide of any of claims 169-172, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

174. A modified oligonucleotide according to the following chemical structure:



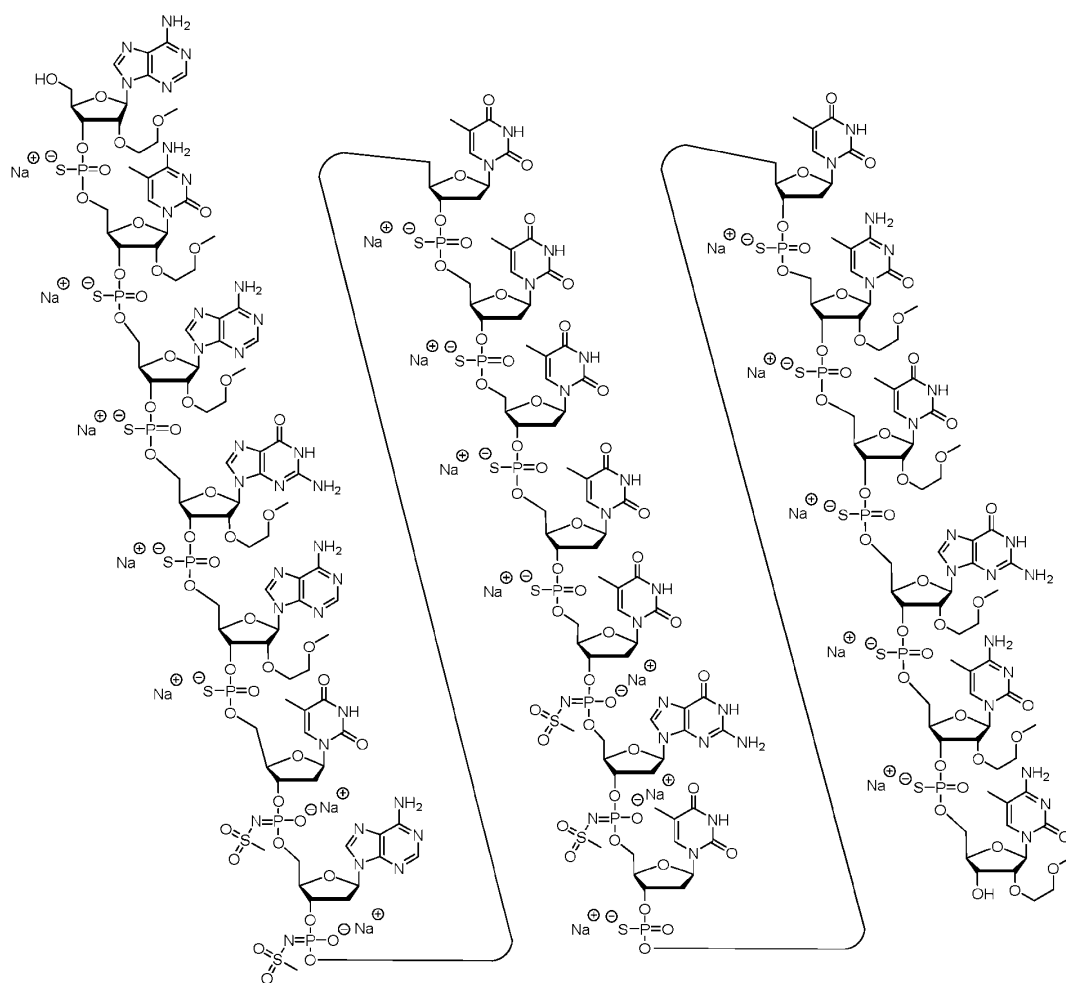
(SEQ ID NO: 3335).

175. A modified oligonucleotide according to the following chemical structure:



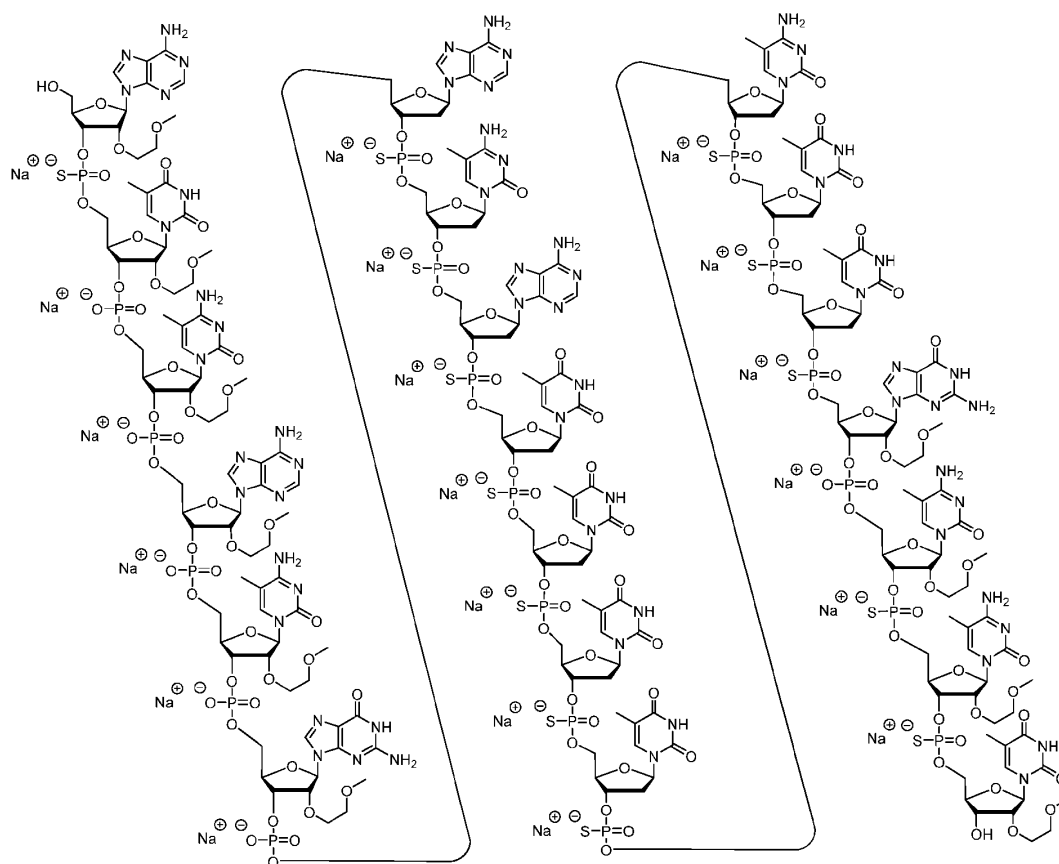
(SEQ ID NO: 3336).

176. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3337).

177. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3338).

178. A population of oligomeric compounds of any of claims 1-135 or a population of modified oligonucleotides of any of claims 169-177, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

179. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*) configuration.

180. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*) configuration.

181. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

182. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides having the (*Sp*) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (*Rp*) configuration at each phosphorothioate internucleoside linkage.

183. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides having the (*Rp*) configuration at one particular phosphorothioate internucleoside linkage and the (*Sp*) configuration at each of the remaining phosphorothioate internucleoside linkages.

184. The population of claim 178, wherein the population is chirally enriched for modified oligonucleotides having at least 3 contiguous phosphorothioate internucleoside linkages in the *Sp*, *Sp*, and *Rp* configurations, in the 5' to 3' direction.
185. A population of oligomeric compounds of any of claims 1-135, modified oligonucleotides of any of claims 169-177, oligomeric duplexes of any of claims 136-164, or antisense agents of any of claims 165-168, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.
186. A population of oligomeric compounds of any of claims 1-135, modified oligonucleotides of any of claims 169-177, oligomeric duplexes of any of claims 136-164, or antisense agents of any of claims 165-168, wherein all of the mesyl phosphoramidate internucleoside linkages of the modified oligonucleotide are stereorandom.
187. A pharmaceutical composition comprising an oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, or a population of any of claims 178-186, and a pharmaceutically acceptable diluent.
188. The pharmaceutical composition of claim 187, wherein the pharmaceutically acceptable diluent is artificial cerebral spinal fluid (aCSF) or phosphate-buffered saline (PBS).
189. The pharmaceutical composition of claim 188, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of claims 1-135, the modified oligonucleotide of any of claims 169-177, the oligomeric duplex of any of claims 136-164, the antisense agent of any of claims 165-168, or the population of any of claims 178-186, and aCSF.
190. The pharmaceutical composition of claim 188, wherein the pharmaceutical composition consists essentially of the oligomeric compound of any of claims 1-135, the modified oligonucleotide of any of claims 169-177, the oligomeric duplex of any of claims 136-164, the antisense agent of any of claims 165-168, or the population of any of claims 178-186, and PBS.
191. A method comprising administering to a subject an oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, a population of any of claims 178-186, or a pharmaceutical composition of any of claims 187-190.
192. The method of claim 191, wherein the subject has or is at risk of developing a synucleinopathy.
193. The method of claim 191, wherein the subject has or is at risk of developing Parkinson's disease.
194. The method of claim 191, wherein the subject has or is at risk of developing multiple system atrophy (MSA).
195. The method of claim 191, wherein the subject has or is at risk of developing dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, neuronopathic Gaucher's disease, or Alzheimer's disease.
196. A method of treating a synucleinopathy comprising administering to a subject having or at risk of developing a synucleinopathy a therapeutically effective amount of an oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, a population of any of claims 178-186, or a pharmaceutical composition of any of claims 187-190.
197. The method of claim 196, wherein the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease.
198. The method of claim 196, wherein the synucleinopathy is Parkinson's disease.

199. The method of claim 196, wherein the synucleinopathy is multiple system atrophy (MSA).
200. The method of any of claims 196-199, wherein at least one symptom or hallmark of synucleinopathy is ameliorated.
201. The method of claim 200, wherein the symptom or hallmark is motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.
202. The method of any of claims 196-201, wherein administering the oligomeric compound of any of claims 1-135, the modified oligonucleotide of any of claims 169-177, the oligomeric duplex of any of claims 136-164, the antisense agent of any of claims 165-168, the population of any of claims 178-186, or the pharmaceutical composition of any of claims 187-190 reduces or delays the onset or progression of motor dysfunction, aggregation of alpha-synuclein, neurodegeneration, cognitive decline, dementia, sleep disorders, hyposmia, autonomic failure, ataxia, hallucination, or seizures.
203. The method of any of claims 191-202, wherein the oligomeric compound of any of claims 1-135, the modified oligonucleotide of any of claims 169-177, the oligomeric duplex of any of claims 136-164, the antisense agent of any of claims 165-168, the population of any of claims 178-186, or the pharmaceutical composition of any of claims 187-190 is administered to the central nervous system or systemically.
204. The method of any of claims 191-203, wherein the oligomeric compound of any of claims 1-135, the modified oligonucleotide of any of claims 169-177, the oligomeric duplex of any of claims 136-164, the antisense agent of any of claims 165-168, the population of any of claims 178-186, or the pharmaceutical composition of any of claims 187-190 is administered intrathecally.
205. The method of any of claims 191-204, wherein the subject is a human.
206. A method of reducing expression of SNCA in a cell comprising contacting the cell with oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, a population of any of claims 178-186, or a pharmaceutical composition of any of claims 187-190.
207. The method of claim 206, wherein the cell is a brain cell.
208. The method of claim 206 or claim 207, wherein the cell is a neuron or an oligodendrocyte.
209. The method of any of claims 206-208, wherein the cell is a human cell.
210. Use of oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, a population of any of claims 178-186, or a pharmaceutical composition of any of claims 187-190 for treating a synucleinopathy.
211. Use of oligomeric compound of any of claims 1-135, a modified oligonucleotide of any of claims 169-177, an oligomeric duplex of any of claims 136-164, an antisense agent of any of claims 165-168, a population of any of claims 178-186, or a pharmaceutical composition of any of claims 187-190 for the manufacture of a medicament for treating a synucleinopathy.
212. The use of claim 210 or claim 211, wherein the synucleinopathy is Parkinson's disease, dementia with Lewy bodies (DLB), diffuse Lewy body disease, Parkinson's disease dementia (PDD), pure autonomic failure, multiple system atrophy (MSA), neuronopathic Gaucher's disease, or Alzheimer's disease.
213. The use of claim 210 or claim 211, wherein the synucleinopathy is Parkinson's disease.

214. The use of claim 210 or claim 211, wherein the synucleinopathy is multiple system atrophy (MSA).