COMPOUNDS AND METHODS FOR REDUCING ATXN3 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 BIOL0331WOSEQ_ST25.txt, created on April 24, 2019, which is 680 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, methods, and pharmaceutical compositions for reducing the amount or activity of ATXN3 RNA in a cell or animal, and in certain instances reducing the amount of Ataxin-3 protein in a cell or animal. Such compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a neurodegenerative disease. Such symptoms and hallmarks include ataxia, neuropathy, and aggregate formation. Such neurodegenerative diseases include spinocerebellar ataxia type 3(SCA3).

Background

Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MJD), is caused by a mutation in the ATXN3 gene and is characterized by progressive cerebellar ataxia and variable findings including a dystonic-rigid syndrome, a parkinsonian syndrome, or a combined syndrome of dystonia and peripheral neuropathy. SCA3 is inherited in an autosomal dominant manner. Offspring of affected individuals have a 50% chance of inheriting the mutation. The diagnosis of SCA3 rests on the use of molecular genetic testing to detect an abnormal CAG trinucleotide repeat expansion in ATXN3. Affected individuals have alleles with 52 to 86 CAG trinucleotide repeats. Such testing detects 100% of affected individuals. Expanded CAG repeats in the ATXN3 gene are translated into expanded polyglutamine repeats (polyQ) in the ataxin-3 protein and this toxic ataxin-3 protein is associated with aggregates. The polyglutamine expanded ataxin-3 protein in these aggregates is ubiquinated and the aggregates contain other proteins, including heat shock proteins and transcription factors. Aggregates are frequently observed in the brain tissue of SCA3 patients. Management of SCA3 is supportive as no medication slows the course of disease; restless legs syndrome and extrapyramidal syndromes resembling parkinsonism may respond to levodopa or dopamine agonists; spasticity, drooling, and sleep problems respond variably to lioresal, atropine-like drugs, and hypnotic agents; botulinum toxin has been used for dystonia and spasticity; daytime fatigue may respond to psychostimulants such as modafinil; accompanying depression should be treated. Riess, O., Rüb, U., Pastore, A. et al. Cerebellum (2008) 7: 125.

Currently there is a lack of acceptable options for treating neurodegenerative diseases such as SCA3. It is therefore an object herein to provide compounds, methods, and pharmaceutical compositions for the treatment of such diseases.

Summary of the Invention

Provided herein are compounds, methods, and pharmaceutical compositions for reducing the amount or activity of ATXN3 RNA, and in certain embodiments reducing the amount of Ataxin-3 protein in a cell or animal. In certain embodiments, the animal has a neurodegenerative disease. In certain embodiments, the animal has SCA3. In certain

embodiments, compounds useful for reducing expression of ATXN3 RNA are oligomeric compounds. In certain embodiments, the oligomeric compound comprises a modified oligonucleotide.

Also provided are methods useful for ameliorating at least one symptom or hallmark of a neurodegenerative disease. In certain embodiments, the neurodegenerative disease is SCA3. In certain embodiments symptoms and hallmarks include ataxia, neuropathy, and aggregate formation. In certain embodiments, amelioration of these symptoms results in improved motor function, reduced neuropathy, and reduction in number of aggregates.

Detailed Description of the Invention

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 in 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, as found in naturally occurring deoxyribonucleic acids (DNA). In certain embodiments, a 2'-deoxynucleoside may comprise a modified nucleobase or may comprise an RNA nucleobase (uracil).

As used herein, "2'-substituted nucleoside" means a nucleoside comprising a 2'-substituted 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-methyl cytosine" means a cytosine modified with a methyl group attached to the 5-position. A 5-methyl cytosine is a modified nucleobase.

As used herein, "administering" means providing a pharmaceutical agent to an animal.

As used herein, "animal" means a human or non-human animal.

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 target nucleic acid levels or target protein levels in the absence of the antisense compound.

As used herein, "antisense compound" means an oligomeric compound capable of achieving at least one antisense activity.

As used herein, "ameliorate" in reference to a treatment means improvement in at least one symptom relative to the same symptom in the absence of the treatment. In certain embodiments, amelioration is the reduction in the severity or frequency of a symptom or the delayed onset or slowing of progression in the severity or frequency of a symptom. In certain embodiments, the symptom or hallmark is ataxia, neuropathy, and aggregate formation. In certain embodiments, amelioration of these symptoms results in improved motor function, reduced neuropathy, or reduction in number of aggregates.

As used herein, "bicyclic nucleoside" or "BNA" means a nucleoside comprising a bicyclic sugar moiety. 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 moiety. In certain embodiments, the bicyclic sugar moiety does not comprise a furanosyl moiety.

As used herein, "cleavable moiety" means a bond or group of atoms that is cleaved under physiological conditions, for example, inside a cell, an animal, 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 regions thereof and the nucleobases of another nucleic acid or one or more regions 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. 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-methyl cytosine (mC) and guanine (G). 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 oligonucleotides means that oligonucleotides are complementary to another oligonucleotide or nucleic acid at each nucleoside of the oligonucleotide.

As used herein, "conjugate group" means a group of atoms that is directly or indirectly attached to an oligonucleotide. Conjugate groups include 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 is attached to an oligonucleotide via a conjugate linker.

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 modified sugar" 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(CH_3)-O-2', and wherein the methyl group of the bridge is in the *S* configuration.

As used herein, "cEt nucleoside" means a nucleoside comprising cEt modified sugar.

As used herein, "chirally enriched 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. 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 compounds comprising modified oligonucleotides.

As used herein, "chirally controlled" in reference to an internucleoside linkage means chirality at that linkage is enriched for a particular stereochemical configuration.

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." Unless otherwise indicated, "gapmer" refers to a sugar motif. Unless otherwise indicated, the sugar moieties of the nucleosides of the gap of a gapmer are unmodified 2'-deoxyribosyl. Thus, the term "MOE gapmer" indicates a gapmer having a sugar motif of 2'-MOE nucleosides in both wings and a gap of 2'-deoxynucleosides. Unless otherwise indicated, a MOE 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 amenable to oligomeric compound-mediated reduction of the amount or activity of the target nucleic acid.

As used herein, "hybridization" means the pairing or annealing of complementary 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.

As used herein, the term "internucleoside linkage" is the covalent linkage between adjacent nucleosides in an oligonucleotide. As used herein "modified internucleoside linkage" means any internucleoside linkage other than a phosphodiester internucleoside linkage. "Phosphorothioate 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, "linker-nucleoside" means a nucleoside that links, either directly or indirectly, an 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, "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, “mismatch” or “non-complementary” means a nucleobase of a first oligonucleotide that is not complementary with the corresponding nucleobase of a second oligonucleotide or target nucleic acid when the first and second oligonucleotide are aligned.

As used herein, “MOE” means methoxyethyl. ”2’-MOE” or “2’-MOE modified sugar” means a 2’-$OCH_2CH_2OCH_3$ group in place of the 2’-OH group of a ribosyl sugar moiety.

As used herein, “2’-MOE nucleoside” means a nucleoside comprising a 2’-MOE modified sugar.

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, “motif” means the pattern of unmodified and/or modified sugar moieties, nucleobases, and/or internucleoside linkages, in an oligonucleotide.

As used herein, “neurodegenerative disease” means a condition marked by progressive loss of structure or function of neurons, including death of neurons. In certain embodiments, neurodegenerative disease is spinocerebellar ataxia type 3 (SCA3).

As used herein, "nucleobase" means an unmodified nucleobase or a modified nucleobase. As used herein an “unmodified nucleobase” is adenine (A), thymine (T), cytosine (C), uracil (U), and 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-methyl cytosine” 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, “nucleoside” means 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. Modified nucleosides include abasic nucleosides, which lack a nucleobase. “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 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 “singled-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 strand 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.

As used herein, “pharmaceutically acceptable carrier or diluent” means any substance suitable for use in administering to an animal. 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, "phosphorus moiety" means a group of atoms comprising a phosphorus atom. In certain embodiments, a phosphorus moiety comprises a mono-, di-, or tri-phosphate, or phosphorothioate.

As used herein "prodrug" means a therapeutic agent in a form outside the body that is converted to a different form within an animal or cells thereof. Typically, conversion of a prodrug within the animal is facilitated by the action of an enzyme (e.g., endogenous or viral enzyme) or chemicals present in cells or tissues and/or by physiologic conditions.

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 compound" means an antisense compound 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 compounds include, but are not limited to double-stranded siRNA, single-stranded RNA (ssRNA), and microRNA, including microRNA mimics. In certain embodiments, an RNAi compound modulates the amount, activity, and/or splicing of a target nucleic acid. The term RNAi compound excludes antisense compounds that act through RNase H.

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

As used herein, "standard cell assay" means the assay described in Example 1 and reasonable variations thereof.

As used herein, "standard in vivo assay' means the experiment described in Example 4 and reasonable variations thereof.

As used herein, "stereorandom" in the context of a population of molecules of identical molecular formula means a chiral center having a random 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 but is not necessarily the same as the number of molecules having the (*R*) configuration of the stereorandom chiral center. The stereochemical configuration of a chiral center is considered random when it is the results of a synthetic method that is not designed to control the stereochemical configuration. In certain embodiments, a stereorandom chiral center is a stereorandom phosphorothioate internucleoside linkage.

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) ribosyl moiety, as found in RNA (an “unmodified RNA sugar moiety”), or a 2’-H(H) 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 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.

As used herein, “target nucleic acid” and “target RNA” mean a nucleic acid that an antisense compound is designed to affect.

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, “therapeutically effective amount” means an amount of a pharmaceutical agent that provides a therapeutic benefit to an animal. For example, a therapeutically effective amount improves a symptom of a disease.

CERTAIN EMBODIMENTS

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

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 90% complementary to an equal length portion of an ATXN3 nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar, a sugar surrogate, and a modified internucleoside linkage.

Embodiment 2. 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 at least 20 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 15-2787.

Embodiment 3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising a portion of 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 at least 20 contiguous nucleobases, wherein the portion is complementary to:

an equal length portion of nucleobases 138-175 of SEQ ID NO: 1;
an equal length portion of nucleobases 392-436 of SEQ ID NO: 1;
an equal length portion of nucleobases 1120-1146 of SEQ ID NO: 1;
an equal length portion of nucleobases 1823-1882 of SEQ ID NO: 1;
an equal length portion of nucleobases 3042-3098 of SEQ ID NO: 1;
an equal length portion of nucleobases 3749-3801 of SEQ ID NO: 1;
an equal length portion of nucleobases 5997-6021 of SEQ ID NO: 1;
an equal length portion of nucleobases 19437-19476 of SEQ ID NO: 2;
an equal length portion of nucleobases 34440-34486 of SEQ ID NO: 2;
an equal length portion of nucleobases 39883-39904 of SEQ ID NO: 2; or
an equal length portion of nucleobases 6597-6618 of SEQ ID NO: 2.

Embodiment 4. The oligomeric compound of any one of embodiments 1-3, wherein the ATXN3 nucleic acid has the nucleobase sequence of any of SEQ ID NOs: 1, 2, 3, 4, or 5.

Embodiment 5. The oligomeric compound of any one of embodiments 1-4, consisting of a single-stranded modified oligonucleotide.

Embodiment 6. The oligomeric compound of any one of embodiments 1-5, wherein at least one internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

Embodiment 7. The oligomeric compound of embodiment 6, wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 8. The oligomeric compound of any one of embodiments 1-5, wherein each internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

Embodiment 9. The oligomeric compound of embodiment 8, wherein each modified internucleoside linkage of the modified oligonucleotide is a phosphorothioate internucleoside linkage.

Embodiment 10. The oligomeric compound of any one of embodiments 1-7, wherein at least one internucleoside linkage of the modified oligonucleotide is a phosphodiester internucleoside linkage.

Embodiment 11. The oligomeric compound of any one of embodiments 1-7 and 10, wherein each internucleoside linkage of the modified oligonucleotide is either a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage.

Embodiment 12. The oligomeric compound of any one of embodiments 1-11, wherein at least one nucleobase of the modified oligonucleotide comprises a modified nucleobase.

Embodiment 13. The oligomeric compound of embodiment 12, wherein the modified nucleobase is a 5-methyl cytosine.

Embodiment 14. The oligomeric compound of any one of embodiments 1-13, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a modified sugar moiety.

Embodiment 15. The oligomeric compound of embodiment 14, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety.

Embodiment 16. The oligomeric compound of embodiment 15, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety having a 2'-4' bridge, wherein the 2'-4' bridge is selected from -O-CH2-; and -O-CH(CH3)-.

Embodiment 17. The oligomeric compound of any of embodiments 1-13, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a non-bicyclic sugar moiety.

Embodiment 18. The oligomeric compound of embodiment 17, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a modified non-bicyclic sugar moiety comprising a 2'-MOE or 2'-OMe.

Embodiment 19. The oligomeric compound of embodiment 18, wherein each modified nucleoside of the modified oligonucleotide comprises a modified non-bicyclic sugar moiety comprising a 2'-MOE or 2'-OMe.

Embodiment 20. The oligomeric compound of any of embodiments 1-13, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.

Embodiment 21. The oligomeric compound of embodiment 20, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate selected from morpholino and PNA.

Embodiment 22. The oligomeric compound of any of embodiments 1-18 and 20-21, wherein the modified oligonucleotide is a gapmer.

Embodiment 23. The oligomeric compound of any of embodiments 1-18 and 20-21, wherein the modified oligonucleotide has a sugar motif comprising:

a 5'-region consisting of 1-6 linked 5'-nucleosides;

a central region consisting of 6-10 linked central region nucleosides; and

a 3'-region consisting of 1-6 linked 5'-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'-deoxyribosyl sugar moiety.

Embodiment 24. The oligomeric compound of embodiments 1-7 or 10-23, wherein the modified oligonucleotide consists of 20 linked nucleosides and has the following internucleoside motif: sooossssssssssssooss; wherein,

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 25. The oligomeric compound of any one of embodiments 1-23, wherein the modified oligonucleotide consists of 12-22, 12-20, 14-20, 16-20, 18-20, or 18-22 linked nucleosides.

Embodiment 26. The oligomeric compound of any one of embodiments 1-23 and 25, wherein the modified oligonucleotide consists of 16, 17, 18, 19, or 20 linked nucleosides.

Embodiment 27. The oligomeric compound of any of embodiments 1-26 consisting of the modified oligonucleotide.

Embodiment 28. The oligomeric compound of any of embodiments 1-26 comprising a conjugate group comprising a conjugate moiety and a conjugate linker.

Embodiment 29. The oligomeric compound of embodiment 28, wherein the conjugate group comprises a GalNAc cluster comprising 1-3 GalNAc ligands.

Embodiment 30. The oligomeric compound of embodiment 28 or 29, wherein the conjugate linker consists of a single bond.

Embodiment 31. The oligomeric compound of embodiment 28, wherein the conjugate linker is cleavable.

Embodiment 32. The oligomeric compound of embodiment 28, wherein the conjugate linker comprises 1-3 linker-nucleosides.

Embodiment 33. The oligomeric compound of any of embodiments 28-32, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

Embodiment 34. The oligomeric compound of any of embodiments 28-32, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 35. The oligomeric compound of any of embodiments 1-26 or 28-34 comprising a terminal group.

Embodiment 36. The oligomeric compound of any of embodiments 1-35 wherein the oligomeric compound is a singled-stranded oligomeric compound.

Embodiment 37. The oligomeric compound of any of embodiments 1-31 or 33-34, wherein the oligomeric compound does not comprise linker-nucleosides.

Embodiment 38. An oligomeric duplex comprising an oligomeric compound of any of embodiments 1-35 and 37.

Embodiment 39. An antisense compound comprising or consisting of an oligomeric compound of any of embodiments 1-37 or an oligomeric duplex of embodiment 38.

Embodiment 40. 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 at least 20 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NOs: 15-2787.

Embodiment 41. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 1-37, an oligomeric duplex of embodiment 38, an antisense compound of embodiment 39, or a modified oligonucleotide of embodiment 40 and at least one of a pharmaceutically acceptable carrier or diluent.

Embodiment 42. The pharmaceutical composition of embodiment 41, wherein the modified oligonucleotide is a sodium salt.

Embodiment 43. A method comprising administering to an animal the pharmaceutical composition of any of embodiments 41-42.

Embodiment 44. The method of embodiment 43, wherein the animal is a human.

Embodiment 45. A method of treating a disease associated with ATXN3 comprising administering to an individual having or at risk for developing a disease associated with ATXN3 a therapeutically effective amount of a pharmaceutical composition of embodiments 41 and 42, and thereby treating the disease associated with ATXN3.

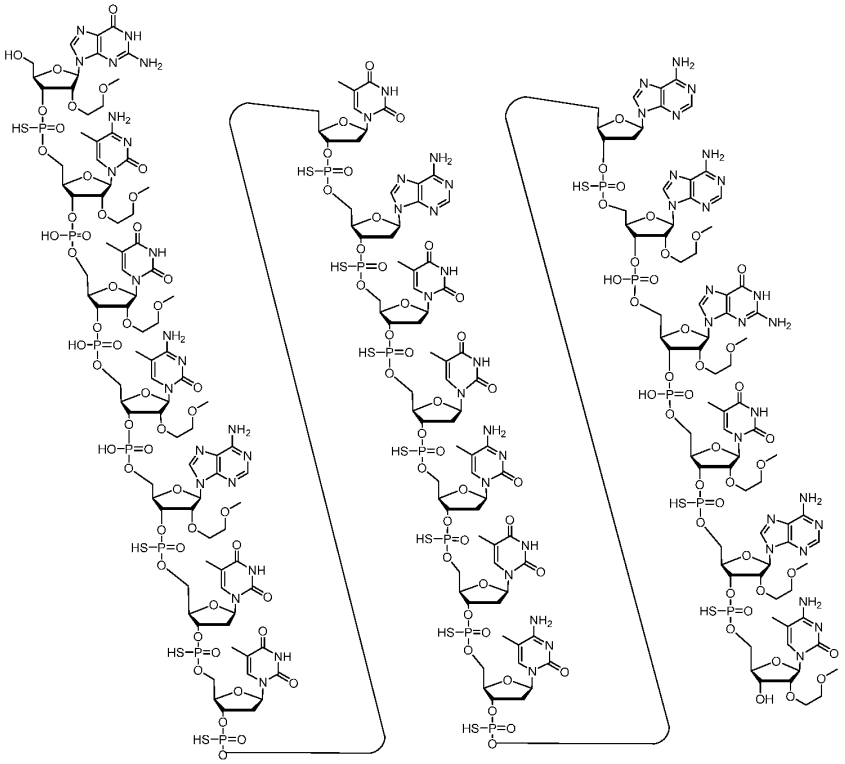
Embodiment 46. The method of embodiment 45, wherein the disease associated with ATXN3 is a neurodegenerative disease.

Embodiment 47. The method of embodiment 46, wherein the neurodegenerative disease is SCA3.

Embodiment 48. The method of embodiment 47, wherein at least one symptom or hallmark of the neurodegenerative disease is ameliorated.

Embodiment 49. The method of embodiment 48, wherein the symptom or hallmark is ataxia, neuropathy, and aggregate formation.

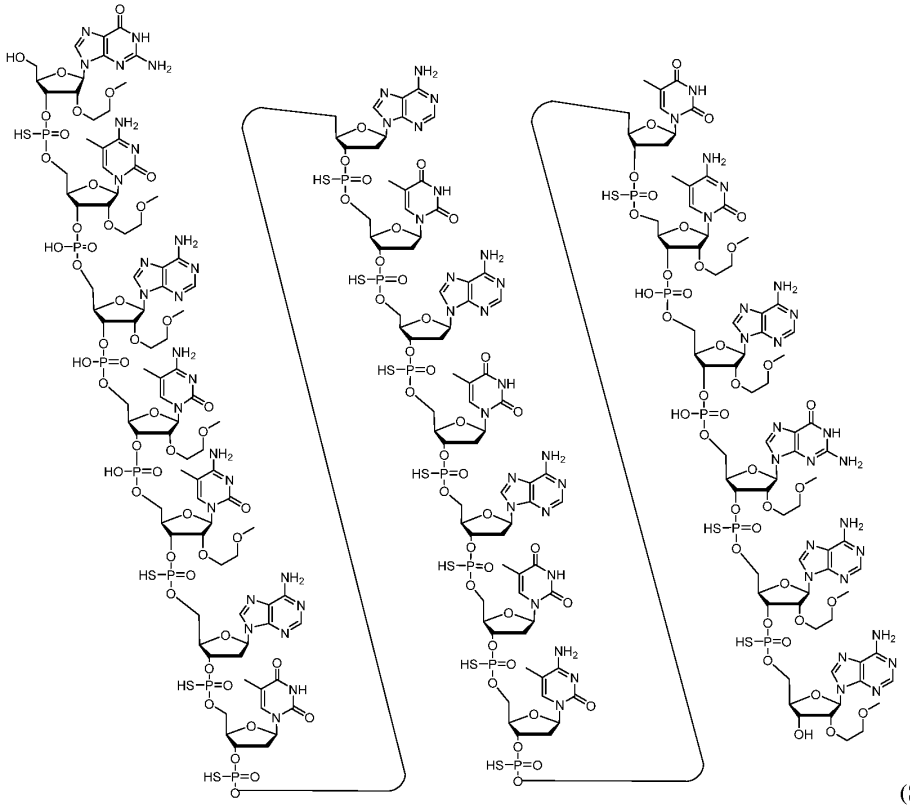
Embodiment 50. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 423),

or a salt thereof.

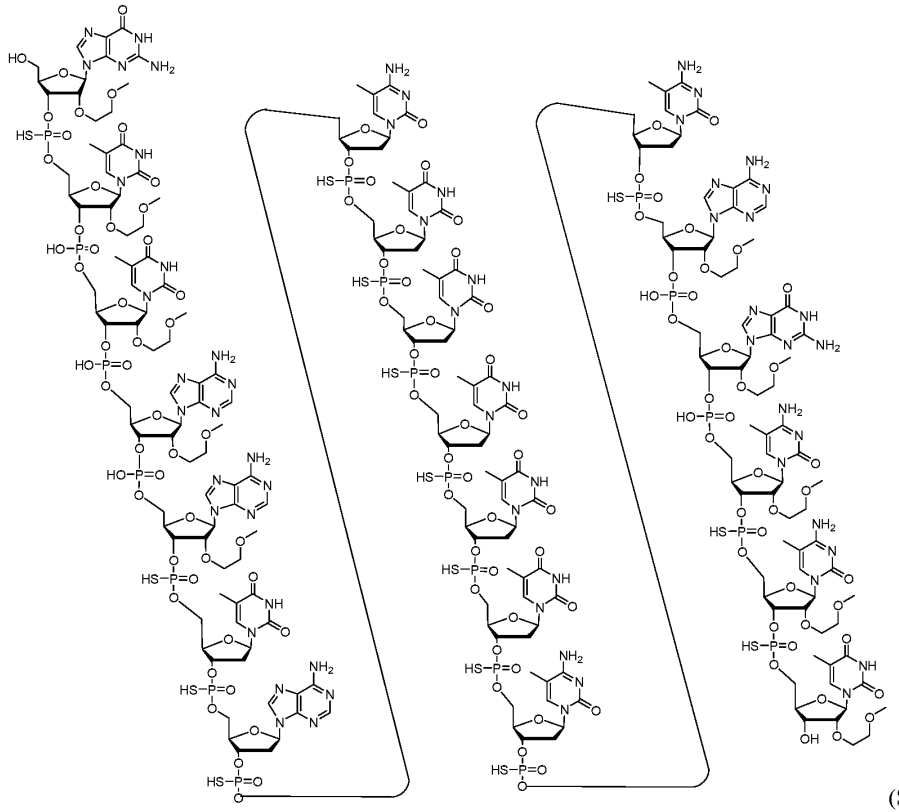
Embodiment 51. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1226),

or a salt thereof.

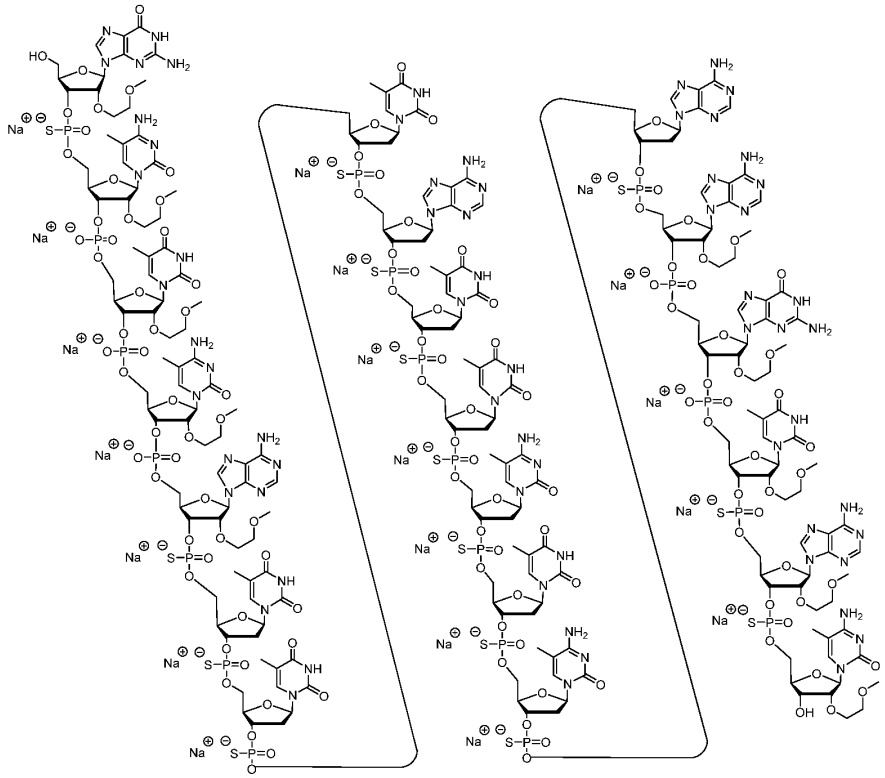
Embodiment 52. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1673),

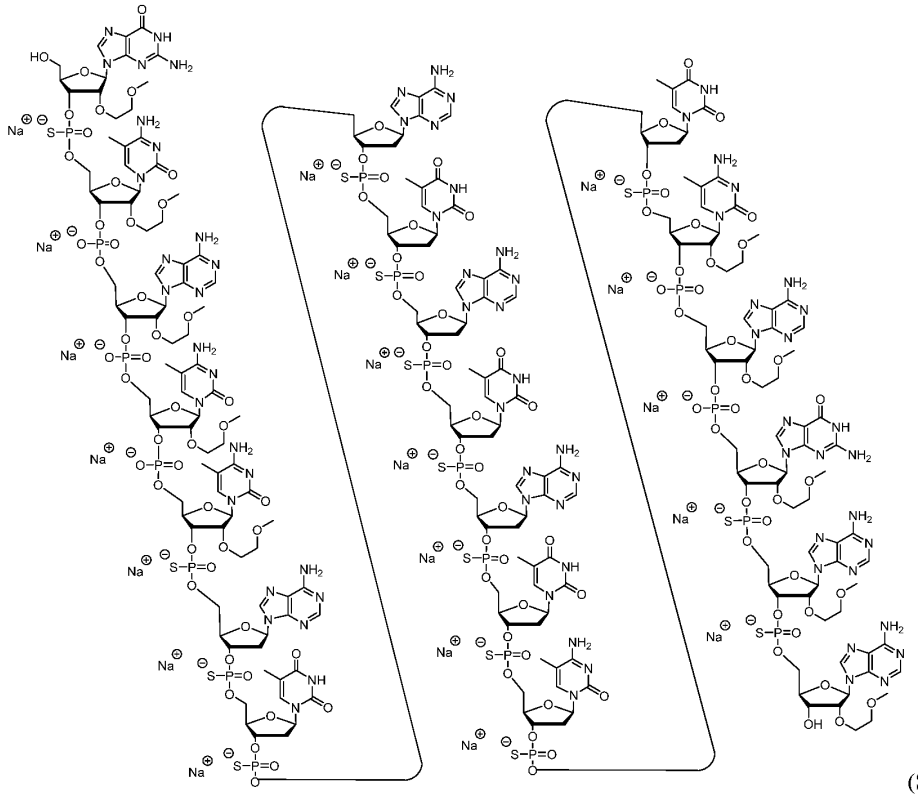
or a salt thereof.

Embodiment 53. A modified oligonucleotide according to the following chemical structure:



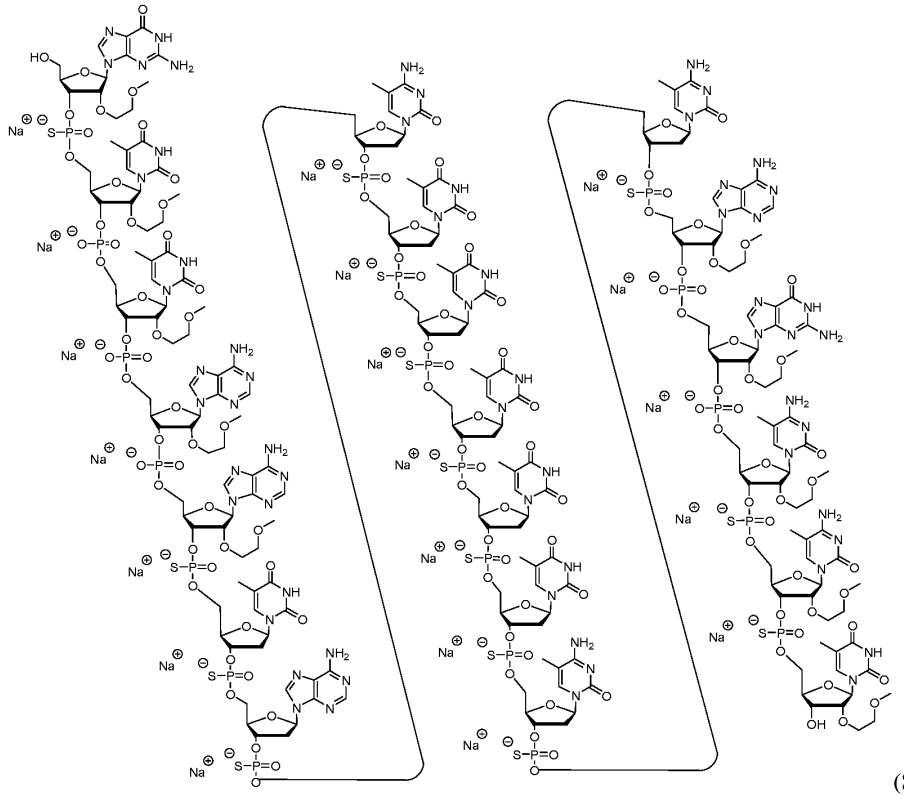
(SEQ ID NO: 423).

Embodiment 54. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1226).

Embodiment 55. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 1673).

Embodiment 56. The modified oligonucleotide of any of embodiments 50, 52, or 54, which is a sodium salt of the formula.

Embodiment 57. A pharmaceutical composition comprising the modified oligonucleotide of any of embodiments 50-56 and a pharmaceutically acceptable carrier or diluent.

Embodiment 58. The pharmaceutical composition of embodiment 57, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid.

Embodiment 59 The pharmaceutical composition of embodiment 57, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebrospinal fluid.

Embodiment 60. A compound comprising a modified oligonucleotide according to the following chemical notation (5' to 3'): Ges ^{m}Ceo Teo ^{m}Ceo Aes Tds Tds Tds Ads Tds Tds ^{m}Cds Tds ^{m}Cds Ads Aeo Geo Tes Aes ^{m}Ce (SEQ ID NO: 423), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

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.

Embodiment 61. A compound comprising a modified oligonucleotide according to the following chemical notation (5' to 3'): Ges ^{m}Ceo Aeo ^{m}Ceo ^{m}Ces Ads Tds Ads Tds Ads Tds Ads Tds ^{m}Cds Tds ^{m}Ceo Aeo Ges Aes Ae (SEQ ID NO: 1226), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

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.

Embodiment 62. A compound comprising a modified oligonucleotide according to the following chemical notation (5' to 3'): Ges Teo Teo Aeo Aes Tds Ads ^{m}Cds Tds Tds Tds Tds Tds ^{m}Cds ^{m}Cds Aeo Geo ^{m}Ces ^{m}Ces Te (SEQ ID NO: 1673), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

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.

Embodiment 63. The compound of any of embodiments 60-62, comprising the modified oligonucleotide covalently linked to a conjugate group.

Embodiment 64. The compound of any of embodiment 1-63, wherein at least one internucleoside linkage of the modified oligonucleotide is chirally controlled.

Embodiment 65. The compound of any of embodiments 1-64, wherein at least one internucleoside linkage of the modified oligonucleotide is stereorandom.

Embodiment 66. A pharmaceutical composition comprising the compound of any of embodiments 60-65 and a pharmaceutically acceptable diluent or carrier.

Embodiment 67. The pharmaceutical composition of embodiment 66, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid.

Embodiment 68. The pharmaceutical composition of embodiment 66, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebrospinal fluid.

Embodiment 69. A chirally enriched population of modified oligonucleotides of any of embodiments 50-55, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

Embodiment 70. The chirally enriched population of embodiment 69, wherein the population is enriched for modified

oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (Sp) configuration.

Embodiment 71. The chirally enriched population of embodiment 69, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (Rp) configuration.

Embodiment 72. The chirally enriched population of embodiment 69, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage

Embodiment 73. The chirally enriched population of embodiment 73, wherein the population is enriched for modified oligonucleotides having the (Sp) configuration at each phosphorothioate internucleoside linkage.

Embodiment 74. The chirally enriched population of embodiment 73, wherein the population is enriched for modified oligonucleotides having the (Rp) configuration at each phosphorothioate internucleoside linkage.

Embodiment 75. The chirally enriched population of embodiment 73, wherein the population is 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 76. The chirally enriched population of embodiment 69 or embodiment 73 wherein the population is 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 77. A chirally enriched population of modified oligonucleotides of any of embodiments 50-55, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

I. Certain Oligonucleotides

In certain embodiments, provided herein are 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.

A. Certain Modified Nucleosides

Modified nucleosides comprise a modified sugar moiety or a modified nucleobase or both a modifed sugar moiety and a modified nucleobase.

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 sugar moieties comprising a furanosyl ring with one or more substituent groups none of which bridges two atoms of the furanosyl ring to form a bicyclic structure. Such non bridging substituents may be at any position of the furanosyl, including but not limited to substituents at the 2', 4', and/or 5' positions. In certain embodiments one or more non-bridging substituent of non-bicyclic modified sugar moieties is branched. Examples of 2'-substituent groups suitable for non-bicyclic modified

sugar moieties include but are not limited to: 2'-F, 2'-OCH_3 ("OMe" or "O-methyl"), and 2'-$O(CH_2)_2OCH_3$ ("MOE"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF_3, OCF_3, O-C_1-C_{10} alkoxy, O-C_1-C_{10} substituted alkoxy, O-C_1-C_{10} alkyl, O-C_1-C_{10} 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, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$ or $OCH_2C(=O)$-$N(R_m)(R_n)$, where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl, 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. 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 (NO_2), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl. Examples of 4'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to alkoxy (*e.g.*, methoxy), alkyl, and those described in Manoharan et al., WO 2015/106128. Examples of 5'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to: 5'-methyl (R or S), 5'-vinyl, and 5'-methoxy. In certain embodiments, non-bicyclic modified sugar moieties comprise more than one non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties and the modified sugar moieties and modified nucleosides described in Migawa et al., WO 2008/101157 and Rajeev et al., US2013/0203836.

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, NH_2, N_3, OCF_3, OCH_3, $O(CH_2)_3NH_2$, $CH_2CH{=}CH_2$, $OCH_2CH{=}CH_2$, $OCH_2CH_2OCH_3$, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$, $O(CH_2)_2O(CH_2)_2N(CH_3)_2$, and N-substituted acetamide ($OCH_2C(=O)$-$N(R_m)(R_n)$), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl.

In certain embodiments, a 2'-substituted nucleoside non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, OCF_3, OCH_3, $OCH_2CH_2OCH_3$, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(CH_3)_2$, $O(CH_2)_2O(CH_2)_2N(CH_3)_2$, and $OCH_2C(=O)$-$N(H)CH_3$ ("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, OCH_3, and $OCH_2CH_2OCH_3$.

Certain modifed 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 such 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'-CH_2-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2-O-2' ("LNA"), 4'-CH_2-S-2', 4'-$(CH_2)_2$-O-2' ("ENA"), 4'-$CH(CH_3)$-O-2' (referred to as "constrained ethyl" or "cEt"), 4'-CH_2-O-CH_2-2', 4'-CH_2-N(R)-2', 4'-$CH(CH_2OCH_3)$-O-2' ("constrained MOE" or "cMOE") and analogs thereof (*see, e.g.,* Seth et al., U.S. 7,399,845, Bhat et al., U.S. 7,569,686, Swayze et al., U.S. 7,741,457, and Swayze et al., U.S. 8,022,193), 4'-$C(CH_3)(CH_3)$-O-2' and analogs thereof (*see, e.g.,*Seth et al., U.S. 8,278,283), 4'-CH_2-$N(OCH_3)$-2' and analogs thereof (*see, e.g.,* Prakash et al., U.S. 8,278,425), 4'-CH_2-O-$N(CH_3)$-2' (*see, e.g.,* Allerson et al., U.S. 7,696,345 and Allerson et al., U.S. 8,124,745), 4'-CH_2-$C(H)(CH_3)$-2' (*see, e.g.,* Zhou, *et al., J. Org. Chem.*,2009, *74*, 118-134), 4'-CH_2-$C(=CH_2)$-2' and analogs thereof (*see e.g.*, Seth et al., U.S. 8,278,426), 4'-$C(R_aR_b)$-N(R)-O-2', 4'-$C(R_aR_b)$-O-N(R)-2', 4'-CH_2-O-N(R)-2', and 4'-CH_2-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C_1-C_{12} alkyl (*see, e.g.* Imanishi et al., U.S. 7,427,672).

In certain embodiments, such 4' to 2' bridges independently comprise from 1 to 4 linked groups independently selected from: -[C(R_a)(R_b)]$_n$-, -[C(R_a)(R_b)]$_n$-O-, -C(R_a)=C(R_b)-, -C(R_a)=N-, -C(=NR_a)-, -C(=O)-, -C(=S)-, -O-, -Si(R_a)$_2$-, -S(=O)$_x$-, and -N(R_a)-;

wherein:

x is 0, 1, or 2;

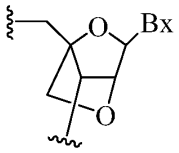
n is 1, 2, 3, or 4;

each R_a and R_b is, independently, H, a protecting group, hydroxyl, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, heterocycle radical, substituted heterocycle radical, heteroaryl, substituted heteroaryl, C_5-C_7 alicyclic radical, substituted C_5-C_7 alicyclic radical, halogen, OJ_1, NJ_1J_2, SJ_1, N_3, COOJ_1, acyl (C(=O)-H), substituted acyl, CN, sulfonyl (S(=O)$_2$-J_1), or sulfoxyl (S(=O)-J_1); and

each J_1 and J_2 is, independently, H, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, acyl (C(=O)-H), substituted acyl, a heterocycle radical, a substituted heterocycle radical, C_1-C_{12} aminoalkyl, substituted C_1-C_{12} aminoalkyl, or a protecting group.

Additional bicyclic sugar moieties are known in the art, see, for example: Freier *et al., Nucleic Acids Research*, 1997, *25*(*22*), 4429-4443, Albaek *et al., J. Org. Chem.*, 2006, *71*, 7731-7740, Singh et al., *Chem. Commun.*, 1998, *4*, 455-456; Koshkin et al., *Tetrahedron*, 1998, *54*, 3607-3630; Kumar et al., *Bioorg. Med. Chem. Lett.*, 1998, *8*, 2219-2222; Singh et al., *J. Org. Chem.*, 1998, *63*, 10035-10039; Srivastava et al., *J. Am. Chem. Soc.*, 20017, *129,* 8362-8379;Wengel et a., U.S. 7,053,207; Imanishi et al., U.S. 6,268,490; Imanishi et al. U.S. 6,770,748; Imanishi et al., U.S. RE44,779; Wengel et al., U.S. 6,794,499; Wengel et al., U.S. 6,670,461; Wengel et al., U.S. 7,034,133; Wengel et al., U.S. 8,080,644; Wengel et al., U.S. 8,034,909; Wengel et al., U.S. 8,153,365; Wengel et al., U.S. 7,572,582; and Ramasamy et al., U.S. 6,525,191;; Torsten et al., WO 2004/106356;Wengel et al., WO 1999/014226; Seth et al., WO 2007/134181; Seth et al., U.S. 7,547,684; Seth et al., U.S. 7,666,854; Seth et al., U.S. 8,088,746; Seth et al., U.S. 7,750,131; Seth et al., U.S. 8,030,467; Seth et al., U.S. 8,268,980; Seth et al., U.S. 8,546,556; Seth et al., U.S. 8,530,640; Migawa et al., U.S. 9,012,421; Seth et al., U.S. 8,501,805; and U.S. Patent Publication Nos. Allerson et al., US2008/0039618 and Migawa et al., US2015/0191727.

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 α-L configuration or in the β-D configuration.



LNA (β-D-configuration)
bridge = 4'-CH_2-O-2'

α-*L*-LNA (α-*L*-configuration)
bridge = 4'-CH_2-O-2'

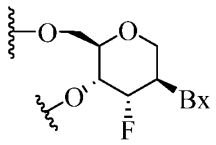
α-L-methyleneoxy (4'-CH_2-O-2') or α-L-LNA bicyclic nucleosides have been incorporated into oligonucleotides that showed antisense activity (Frieden et al., *Nucleic Acids Research,* 2003, *21*, 6365-6372). Herein, general descriptions of bicyclic nucleosides include both isomeric configurations. When the positions of specific bicyclic nucleosides (*e.g.*,

LNA or cEt) are identified in exemplified embodiments herein, they are in the β-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'-2' bridged sugars).

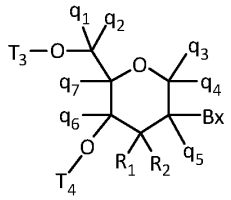
In certain embodiments, modified sugar moieties are sugar surrogates. In certain such embodiments, the oxygen atom of the sugar moiety is replaced, *e.g.,* with a sulfur, carbon or nitrogen atom. In certain such embodiments, such modified sugar moieties also comprise bridging and/or non-bridging substituents as described herein. For example, certain sugar surrogates comprise a 4'-sulfur atom and a substitution at the 2'-position (*see*, *e.g.,* Bhat et al., U.S. 7,875,733 and Bhat et al., U.S. 7,939,677) and/or the 5' position.

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") (*see, e.g.,* Leumann, CJ. *Bioorg. & Med. Chem.* 2002, *10*, 841-854), fluoro HNA:



F-HNA

("F-HNA", *see e.g.*Swayze et al., U.S. 8,088,904; Swayze et al., U.S. 8,440,803; Swayze et al., U.S. 8,796,437; and Swayze et al., U.S. 9,005,906; 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:



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

Bx is a nucleobase moiety;

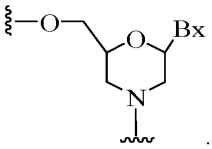
T_3 and T_4 are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T_3 and T_4 is an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T_3 and T_4 is H, a hydroxyl protecting group, a linked conjugate group, or a 5' or 3'-terminal group;

q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each, independently, H, C_1-C_6 alkyl, substituted C_1-C_6 alkyl, C_2-C_6 alkenyl, substituted C_2-C_6 alkenyl, C_2-C_6 alkynyl, or substituted C_2-C_6 alkynyl; and

each of R_1 and R_2 is independently selected from among: hydrogen, halogen, substituted or unsubstituted alkoxy, NJ_1J_2, SJ_1, N_3, $OC(=X)J_1$, $OC(=X)NJ_1J_2$, $NJ_3C(=X)NJ_1J_2$, and CN, wherein X is O, S or NJ_1, and each J_1, J_2, and J_3 is, independently, H or C_1-C_6 alkyl.

In certain embodiments, modified THP nucleosides are provided wherein q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is other than H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is methyl. In certain embodiments, modified THP nucleosides are provided wherein one of R_1 and R_2 is F. In certain embodiments, R_1 is F and R_2 is H, in certain embodiments, R_1 is methoxy and R_2 is H, and in certain embodiments, R_1 is methoxyethoxy and R_2 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 (*see, e.g.,* Braasch et al., Biochemistry, 2002, *41*, 4503-4510 and Summerton et al., U.S. 5,698,685; Summerton et al., U.S. 5,166,315; Summerton et al., U.S. 5,185,444; and Summerton et al., U.S. 5,034,506). As used here, the term "morpholino" means a sugar surrogate having the following structure:



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 refered to herein as "modifed morpholinos."

In certain embodiments, sugar surrogates comprise acyclic moieites. Examples of nucleosides and oligonucleotides comprising such acyclic sugar surrogates include but are not limited to: peptide nucleic acid ("PNA"), acyclic butyl nucleic acid (*see, e.g.,* Kumar et al., *Org. Biomol. Chem.*, 2013, *11*, 5853-5865), and nucleosides and oligonucleotides described in Manoharan et al., WO2011/133876.

Many other bicyclic and tricyclic sugar and sugar surrogate ring systems are known in the art that can be used in modified nucleosides).

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 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: 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-CH_3) uracil, 5-propynylcytosine, 6-azouracil, 6-azocytosine, 6-azothymine, 5-ribosyluracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl, 8-aza and other 8-substituted purines, 5-halo, particularly 5-bromo, 5-trifluoromethyl, 5-halouracil, and 5-halocytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-aminoadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 6-N-benzoyladenine, 2-N-isobutyrylguanine, 4-N-benzoylcytosine, 4-N-benzoyluracil, 5-methyl 4-N-benzoylcytosine, 5-

methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. 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 Merigan et al., U.S. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990, 858-859; Englisch *et al.*, *Angewandte Chemie*, International Edition, 1991, *30*, 613; Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, Crooke, S.T. and Lebleu, B., Eds., CRC Press, 1993, 273-288; and those disclosed in Chapters 6 and 15, *Antisense Drug Technology*, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

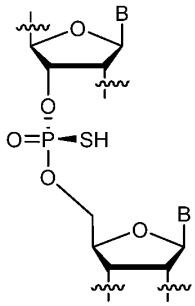
Publications that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include without limitation, Manoharan et al., US2003/0158403; Manoharan et al., US2003/0175906; Dinh et al., U.S. 4,845,205; Spielvogel et al., U.S. 5,130,302; Rogers et al., U.S. 5,134,066; Bischofberger et al., U.S. 5,175,273; Urdea et al., U.S. 5,367,066; Benner et al., U.S. 5,432,272; Matteucci et al., U.S. 5,434,257; Gmeiner et al., U.S. 5,457,187; Cook et al., U.S. 5,459,255; Froehler et al., U.S. 5,484,908; Matteucci et al., U.S. 5,502,177; Hawkins et al., U.S. 5,525,711; Haralambidis et al., U.S. 5,552,540; Cook et al., U.S. 5,587,469; Froehler et al., U.S. 5,594,121; Switzer et al., U.S. 5,596,091; Cook et al., U.S. 5,614,617; Froehler et al., U.S. 5,645,985; Cook et al., U.S. 5,681,941; Cook et al., U.S. 5,811,534; Cook et al., U.S. 5,750,692; Cook et al., U.S. 5,948,903; Cook et al., U.S. 5,587,470; Cook et al., U.S. 5,457,191; Matteucci et al., U.S. 5,763,588; Froehler et al., U.S. 5,830,653; Cook et al., U.S. 5,808,027; Cook et al., 6,166,199; and Matteucci et al., U.S. 6,005,096.

3. Certain Modified Internucleoside Linkages

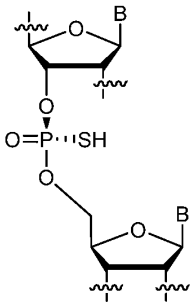
In certain embodiments, nucleosides of modified oligonucleotides may be linked together using any internucleoside linkage. The two main classes of internucleoside linking groups are defined by the presence or absence of a phosphorus atom. Representative phosphorus-containing internucleoside linkages include but are not limited to phosphates, which contain a phosphodiester bond ("P=O") (also referred to as unmodified or naturally occurring linkages), phosphotriesters, methylphosphonates, phosphoramidates, and phosphorothioates ("P=S"), and phosphorodithioates ("HS-P=S"). Representative non-phosphorus containing internucleoside linking groups include but are not limited to methylenemethylimino ($-CH_2-N(CH_3)-O-CH_2-$), thiodiester, thionocarbamate (-O-C(=O)(NH)-S-); siloxane ($-O-SiH_2-O-$); and N,N'-dimethylhydrazine ($-CH_2-N(CH_3)-N(CH_3)-$). Modified internucleoside linkages, compared to naturally occurring phosphate 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.

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 phosphorothioate 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. Such modified oligonucleotides can be generated using synthetic methods that result in random selection of the stereochemical configuration of each phosphorothioate linkage. Nonetheless, as is well understood by those of skill in the art, each individual phosphorothioate 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 internucleoside linkages in a particular, independently selected stereochemical configuration. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 65% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 70% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 80% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 90% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate 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. *Nuc. Acid. 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 in the (*S*p) configuration. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one phosphorothioate in the (*R*p) configuration. 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:



(R_p)



(S_p)

Unless otherwise indicated, chiral internucleoside linkages of modified oligonucleotides described herein can be stereorandom or in a particular stereochemical configuration.

Neutral internucleoside linkages include, without limitation, phosphotriesters, methylphosphonates, MMI (3'-CH_2-N(CH_3)-O-5'), amide-3 (3'-CH_2-C(=O)-N(H)-5'), amide-4 (3'-CH_2-N(H)-C(=O)-5'), formacetal (3'-O-CH_2-O-5'), methoxypropyl, and thioformacetal (3'-S-CH_2-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 CH_2 component parts.

B. <u>Certain Motifs</u>

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 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 1-5 nucleosides. In certain embodiments, each nucleoside of each wing of a gapmer is a modified nucleoside. In certain embodiments, each nucleoside of each wing of a gapmer is a modified nucleoside. In certain embodiments, at least one nucleoside of each wing of a gapmer is a modified nucleoside. In certain embodiments, at least two nucleosides of each wing of a gapmer are modified nucleosides. In certain embodiments, at least three nucleosides of each wing of a gapmer are modified nucleosides. In certain embodiments, at least four nucleosides of each wing of a gapmer are modified nucleosides.

In certain embodiments, the gap of a gapmer comprises 7-12 nucleosides. In certain embodiments, each nucleoside of the gap of a gapmer is an unmodified 2'-deoxy nucleoside.

In certain embodiments, the gapmer is a deoxy gapmer. In embodiments, the nucleosides on the gap side of each wing/gap junction are unmodified 2'-deoxy nucleosides and the nucleosides on the wing sides of each wing/gap junction are modified nucleosides. In certain embodiments, each nucleoside of the gap is an unmodified 2'-deoxy nucleoside. In certain embodiments, each nucleoside of each wing of a gapmer is a modified nucleoside.

In certain embodiments, modified oligonucleotides comprise or consist of a region having a fully modified sugar motif. In such embodiments, each nucleoside of the fully modified region 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 region having a fully modified sugar motif, wherein each nucleoside within the fully modified region 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 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 5-10-5 gapmer consists of 5 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 unmodified deoxynucleosides sugars. Thus, a 5-10-5 MOE gapmer consists of 5 linked MOE modified nucleosides in the 5'-wing, 10 linked deoxynucleosides in the gap, and 5 linked MOE nucleosides in the 3'-wing.

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.

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 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-methyl cytosines. In certain embodiments, all of the cytosine nucleobases are 5-methyl cytosines 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'-deoxyribosyl moiety. In certain embodiments, the modified nucleobase is selected from: a 2-thiopyrimidine and a 5-propynepyrimidine.

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 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 a (*S*p) phosphorothioate, and a (*R*p) 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 such 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 (*S*p) phosphorothioates, and the gap comprises at least one *S*p, *S*p, *R*p motif. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising such internucleoside linkage motifs.

C. Certain Lengths

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≤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 29, 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

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 (unmodified or modified oligonucleotides) are further described by their nucleobase sequence. In certain embodiments oligonucleotides have a nucleobase sequence that is complementary to a second oligonucleotide or an identified reference nucleic acid, such as a target nucleic acid. In certain such embodiments, a region of an oligonucleotide has a nucleobase sequence that is complementary to a second oligonucleotide or an identified reference nucleic acid, 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 nucleic acid, such as a target nucleic acid.

II. Certain Oligomeric Compounds

In certain embodiments, provided herein are oligomeric compounds, which consist of an oligonucleotide (modified or unmodified) and optionally one or more conjugate groups and/or terminal groups. Conjugate groups consist of one or more 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 that are attached to either or both ends of an oligonucleotide are terminal groups. In certain such embodiments, conjugate groups or terminal groups are attached at the 3' and/or 5'-end of oligonucleotides.

In certain such embodiments, conjugate groups (or terminal groups) are attached at the 3'-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 3'-end of oligonucleotides. In certain embodiments, conjugate groups (or terminal groups) are attached at the 5'-end of oligonucleotides. In certain embodiments, conjugate groups are attached near the 5'-end of oligonucleotides.

Examples of terminal groups include but are not limited to conjugate groups, capping groups, phosphate moieties, protecting groups, modified or unmodified nucleosides, and two or more nucleosides that are independently modified or unmodified.

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, 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., *Nucl. 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., *Nucl. 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).

1. Conjugate Moieties

Conjugate moieties include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates, vitamin moieties, polyethylene glycols, thioethers, polyethers, cholesterols, 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-triiodobenzoic acid, fingolimod, flufenamic acid, folinic acid, a benzothiadiazide, chlorothiazide, a diazepine, indo-methicin, a barbiturate, a cephalosporin, a sulfa drug, an antidiabetic, an antibacterial or an antibiotic.

2. Conjugate Linkers

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 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 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 parent compounds, such as the oligonucleotides provided herein. In general, a bifunctional linking moiety comprises at least two functional groups. One of the functional groups is selected to bind to a particular site on a parent 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.

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-aminohexanoic acid (AHEX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C_1-C_{10} alkyl, substituted or unsubstituted C_2-C_{10} alkenyl or substituted or unsubstituted C_2-C_{10} 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-methyl cytosine, 4-N-benzoyl-5-methyl cytosine, 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.

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'-deoxy nucleoside 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 embodiments, the cleavable moiety is 2'-deoxyadenosine.

B. Certain Terminal Groups

In certain embodiments, oligomeric compounds comprise one or more terminal groups. In certain such embodiments, oligomeric compounds comprise a stabilized 5'-phophate. Stabilized 5'-phosphates include, but are not limited to 5'-phosphanates, including, but not limited to 5'-vinylphosphonates. In certain embodiments, terminal groups comprise one or more abasic nucleosides and/or inverted nucleosides. In certain embodiments, terminal groups comprise one or more 2'-linked nucleosides. In certain such embodiments, the 2'-linked nucleoside is an abasic nucleoside.

III. Oligomeric Duplexes

In certain embodiments, oligomeric compounds described herein comprise an oligonucleotide, having a nucleobase sequence complementary to that of a target nucleic acid. In certain embodiments, an oligomeric compound is paired with a second oligomeric compound to form an oligomeric duplex. Such oligomeric duplexes comprise a first oligomeric compound having a region complementary to a target nucleic acid and a second oligomeric compound having a region complementary to the first oligomeric compound. In certain embodiments, the first oligomeric compound of an oligomeric duplex comprises or consists of (1) a modified or unmodified oligonucleotide and optionally a conjugate group and (2) a second modified or unmodified oligonucleotide and optionally a conjugate group. Either or both oligomeric compounds of an oligomeric duplex may comprise a conjugate group. The oligonucleotides of each oligomeric compound of an oligomeric duplex may include non-complementary overhanging nucleosides.

IV. Antisense Activity

In certain embodiments, oligomeric compounds and oligomeric duplexes are capable of hybridizing to a target nucleic acid, resulting in at least one antisense activity; such oligomeric compounds and oligomeric duplexes are antisense compounds. In certain embodiments, antisense compounds have antisense activity when they reduce or inhibit the amount or activity of a target nucleic acid by 25% or more in the standard cell 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 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.

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 compounds. RNAi compounds may be double-stranded (siRNA) or single-stranded (ssRNA).

In certain embodiments, hybridization of an antisense compound to a target nucleic acid does not result in 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.

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 animal.

V. 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 RNA 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 such 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 such 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

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 (Nuc. Acid. 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 that 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.

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, the 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. ATXN3

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 ATXN3. In certain embodiments, ATXN3 nucleic acid has the sequence set forth in SEQ ID NO: 1 (GENBANK Accession No: NM_004993.5); SEQ ID

NO: 2 (the complement of GENBANK Accession No NC_000014.9 truncated from nucleotides 92,056,001 to 92,110,000); SEQ ID NO: 3 (GENBANK Accession No: NM_001164781.1); SEQ ID NO: 4 (GENBANK Accession No: NM_001127697.2); and SEQ ID NO: 5 (ensemble transcript No: ENST00000558190.5).

In certain embodiments, contacting a cell with an oligomeric compound complementary to any of SEQ ID NOs: 1-5 reduces the amount of ATXN3 RNA, and in certain embodiments reduces the amount of Ataxin-3 protein. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, contacting a cell in an animal with an oligomeric compound complementary to any of SEQ ID NOs: 1-5 ameliorate one or more symptom or hallmark of a neurodegenerative disease. In certain embodiments, the symptom or hallmark is ataxia, neuropathy, and aggregate formation. In certain embodiments, contacting a cell in an animal with an oligonucleotide complementary to any of SEQ ID Nos: 1-5 results in improved motor function, reduced neuropathy, and/or reduction in number of aggregates. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide.

C. Certain Target Nucleic Acids in Certain Tissues

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 tissues are the cells and tissues that comprise the central nervous system (CNS), including spinal cord, cortex, cerebellum, brain stem, and pons.

VI. Certain Pharmaceutical Compositions

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 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. In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

In certain embodiments, a pharmaceutical composition comprises a modified oligonucleotide and artificial cerebrospinal fluid. 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, 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 an animal, 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. Suitable pharmaceutically acceptable salts include, but are not limited to, sodium and potassium 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.

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. Aqueous injection suspensions may contain.

Under certain conditions, certain compounds disclosed herein act as acids. Although such compounds may be drawn or described in protonated (free acid) form, in ionized (anion) 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 phosphate 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 salts thereof" expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with a cation. In certain instances, one or more specific cation is identified.

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

VII. Certain Compositions

1. Compound No. 1100673

In certain embodiments, Compound No. 1100673 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GCTCATTTATTCTCAAGTAC (SEQ ID NO: 423), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') comprise a 2'-MOE sugar moiety and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 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, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1100673 is represented by the following chemical notation (5' to 3'):

Ges ^{m}Ceo Teo ^{m}Ceo Aes Tds Tds Tds Ads Tds Tds ^{m}Cds Tds ^{m}Cds Ads Aeo Geo Tes Aes ^{m}Ce (SEQ ID NO: 423), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

G = a guanine nucleobase,

T = a thymine nucleobase,

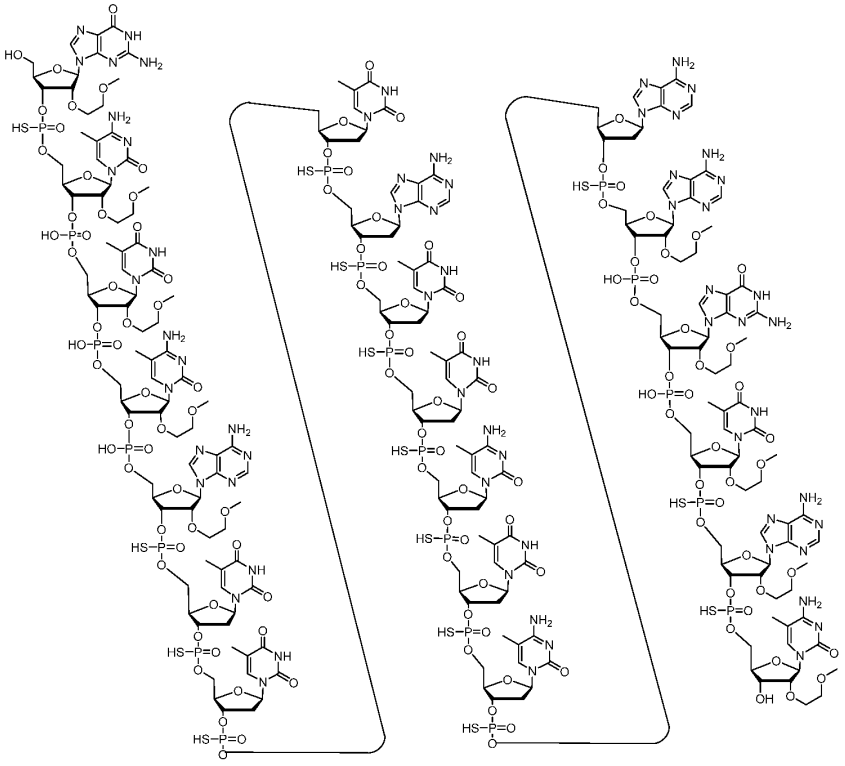
e = a 2' MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

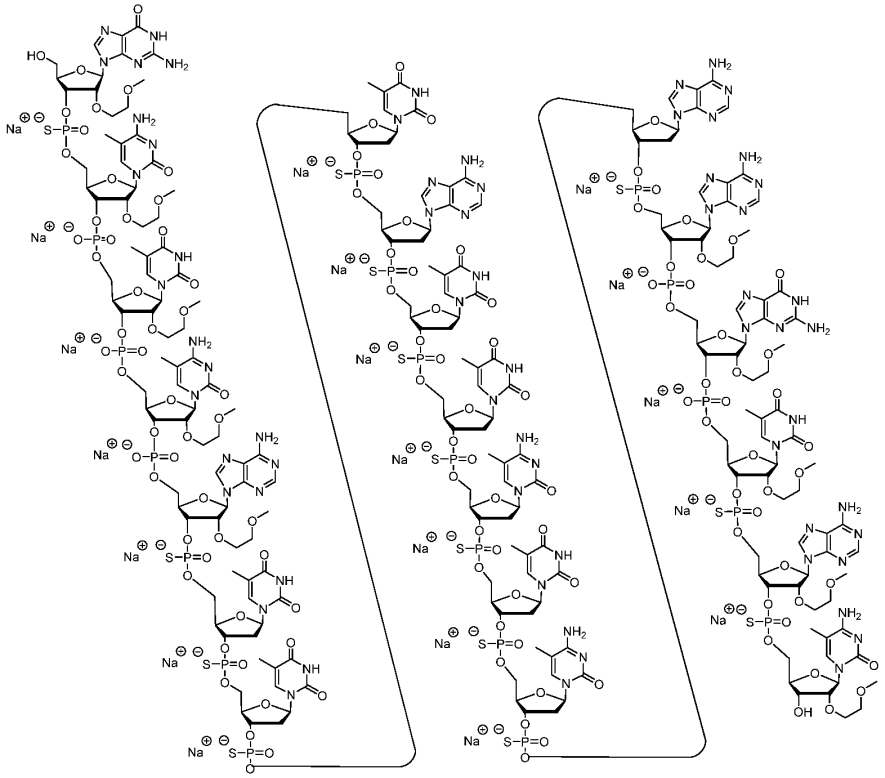
In certain embodiments, Compound No. 1100673 is represented by the following chemical structure:



(SEQ ID NO: 423).

Structure 1. Compound No. 1100673

In certain embodiments, the sodium salt of Compound No. 1100673 is represented by the following chemical structure:



(SEQ ID NO: 423).

Structure 2. The sodium salt of Compound No. 1100673

2. Compound No. 1101657

In certain embodiments, Compound No. 1101657 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GCACCATATATATCTCAGAA (SEQ ID NO: 1226), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') comprise a 2'-MOE sugar moiety and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides (from 5' to 3'), wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages (from 5' to 3') and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 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, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages (from 5' to 3'), and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1101657 is represented by the following chemical notation (5' to 3'): Ges ^{m}Ceo Aeo ^{m}Ceo ^{m}Ces Ads Tds Ads Tds Ads Tds Ads Tds ^{m}Cds Tds ^{m}Ceo Aeo Ges Aes Ae (SEQ ID NO: 1226), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

G = a guanine nucleobase,

T = a thymine nucleobase,

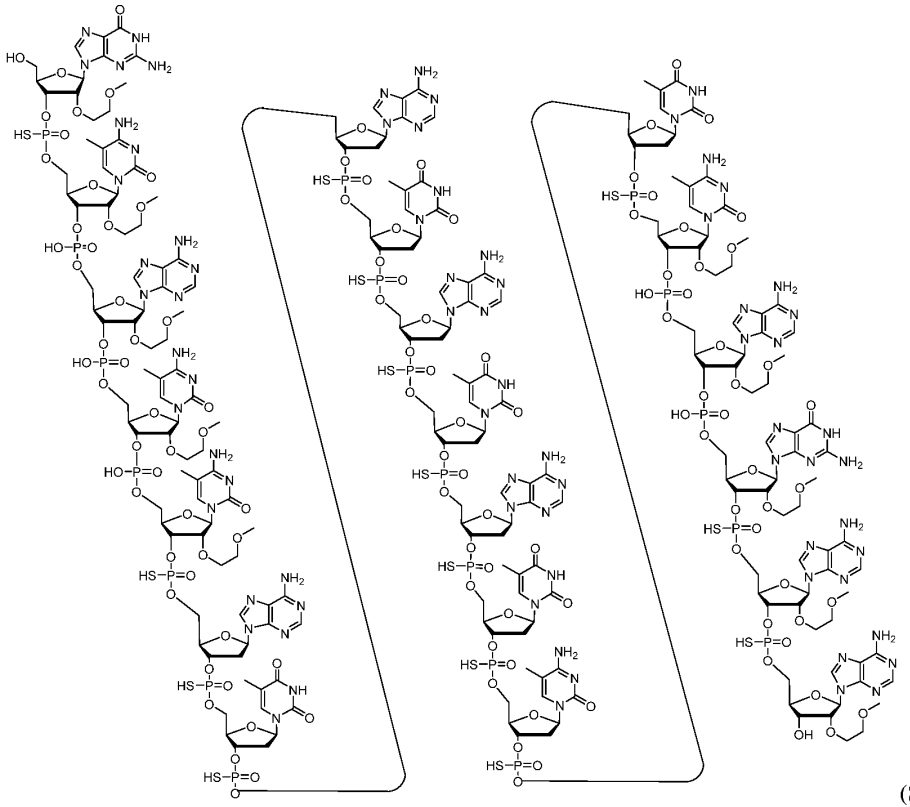
e = a 2' MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

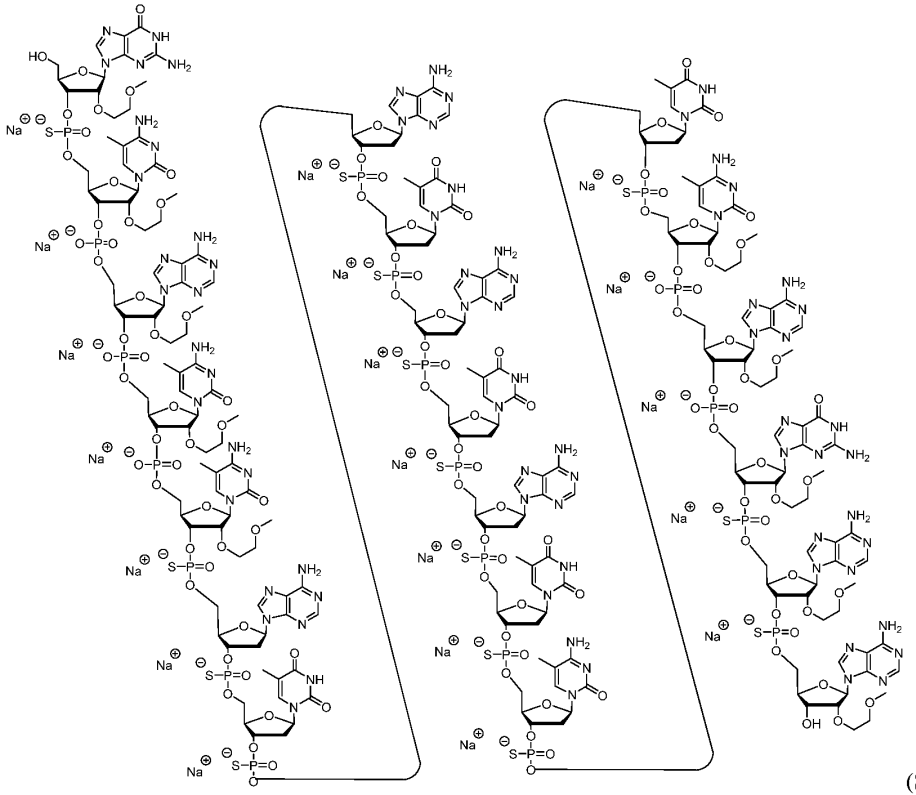
In certain embodiments, Compound No. 1101657 is represented by the following chemical structure:



(SEQ ID NO: 1226).

Structure 3. Compound No. 1101657

In certain embodiments, the sodium salt of Compound No. 1101657 is represented by the following chemical structure:



(SEQ ID NO: 1226).

Structure 4. The sodium salt of Compound No. 1101657

3. Compound No. 1102130

In certain embodiments, Compound No. 1102130 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GTTAATACTTTTTCCAGCCT (SEQ ID NO: 1673), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') comprise a 2'-MOE sugar moiety and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides (from 5' to 3'), wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages (from 5' to 3') and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 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, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages (from 5' to 3'), and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1102130 is represented by the following chemical notation (5' to 3'): Ges Teo Teo Aeo Aes Tds Ads ^{m}Cds Tds Tds Tds Tds Tds ^{m}Cds ^{m}Cds Aeo Geo ^{m}Ces ^{m}Ces Te (SEQ ID NO: 1673), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine,

G = a guanine nucleobase,

T = a thymine nucleobase,

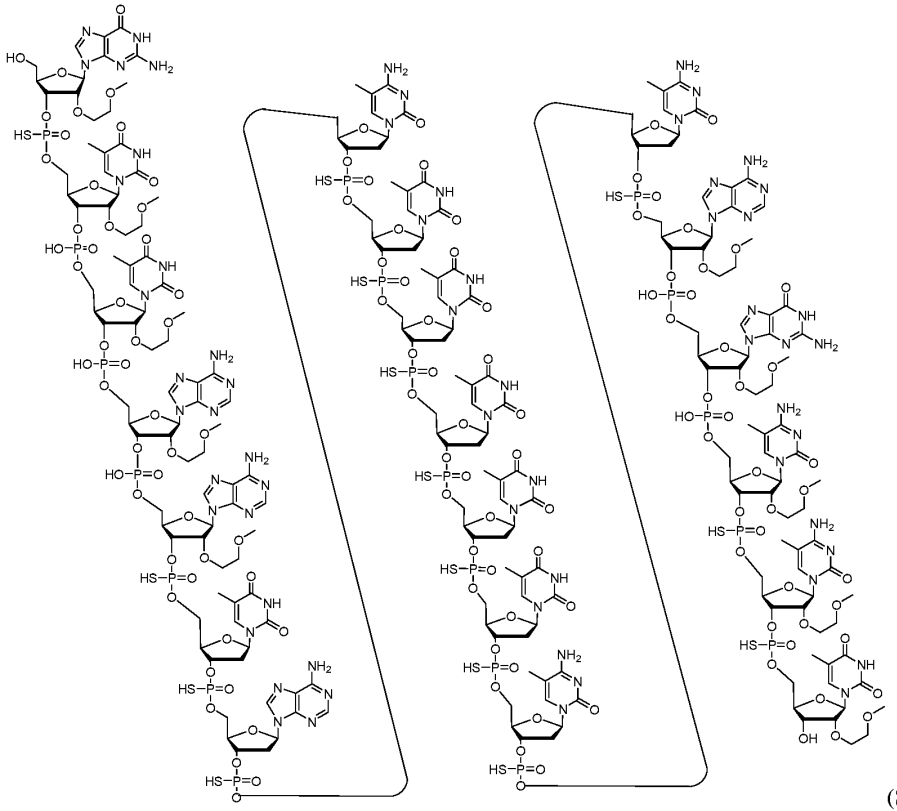
e = a 2' MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

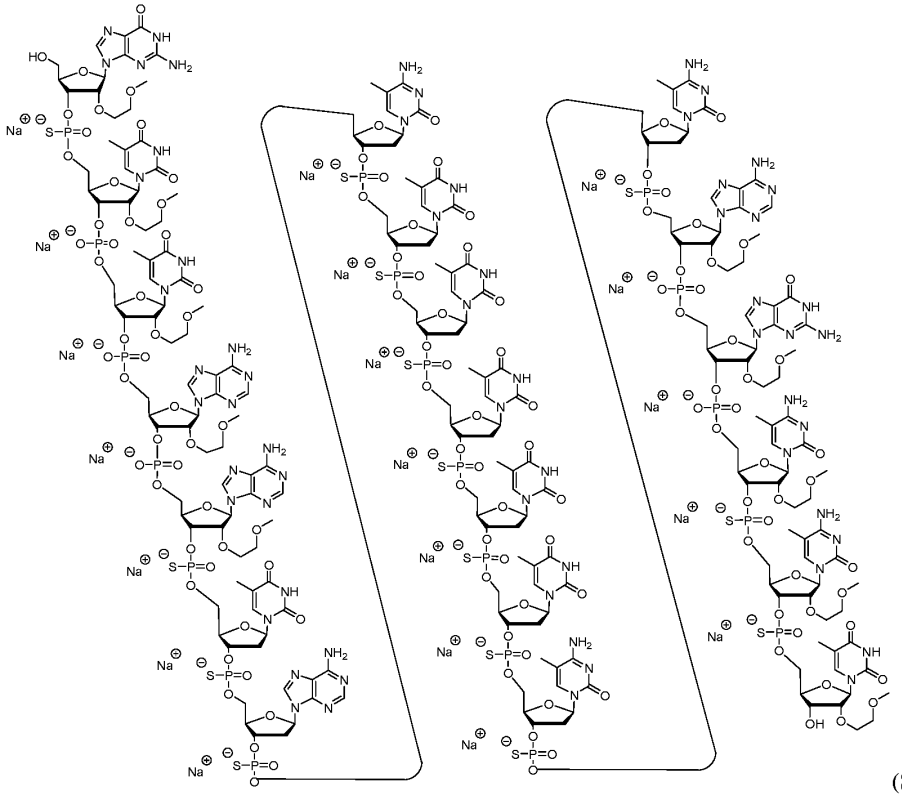
In certain embodiments, Compound No. 1102130 is represented by the following chemical structure:



(SEQ ID NO: 1673).

Structure 5. Compound No. 1102130

In certain embodiments, the sodium salt of Compound No. 1102130 is represented by the following chemical structure:



(SEQ ID NO: 1673).

Structure 6. The sodium salt of Compound No. 1102130

VIII. Certain Comparator Compositions

In certain embodiments, Compound No. 650528, which has been described in Moore, et al., Mol. Ther. Nucleic Acids, 2017, 7:200-210 (Moore, 2017) ("ASO-5"), WO 2018/089805, and McLoughlin et al., Ann. Neurol., 2018, 84:64-77 (McLoughlin, 2018) (each of which are incorporated herein by reference) was used as a comparator compound. Compound No. 650528 is a 5-8-5 MOE gapmer, having a sequence (from 5' to 3') GCATCTTTTCATACTGGC (SEQ ID NO: 2788), wherein each cytosine is a 5'-methylcytosine, each internucleoside linkage is either a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage and the internucleoside linkage motif is sooossssssssssooss, wherein 's' represents a phosphorothioate internucleoside linkage and 'o' represents a phosphodiester internucleoside linkage, and wherein each of nucleosides 1-5 and 14-18 comprise a 2'-MOE sugar moiety.

In certain embodiments, Compound No. 650668, which has been described in Moore, 2017 ("ASO-2"), WO 2018/089805, and McLoughlin, 2018 was used as a comparator compound. Compound No. 650668, is a 5-8-5 MOE gapmer, having a sequence (from 5' to 3') AGCCATTAATCTATACTG (SEQ ID NO: 2792), wherein each cytosine is a 5'-methylcytosine, each internucleoside linkage is either a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage and the internucleoside linkage motif is sooossssssssssooss, wherein 's' represents a phosphorothioate internucleoside linkage and 'o' represents a phosphodiester internucleoside linkage, and

wherein each of nucleosides 1-5 and 14-18 comprise a 2'-MOE sugar moiety.

Compound No. 650528 and Compound No. 650668 were selected as comparator compounds because according to Moore, 2017 these compounds were "top ASO candidates" that were effective and tolerable. See, e.g., page 206, column 2, paragraph 1. In a follow up manuscript, Compound No. 650528 was further characterized as "…the best ASO candidate…[f]rom this short-term safety and efficacy study…" See, McLoughlin, 2018.

In certain embodiments, Compound No. 1244463 ("SH06"), which has been described in WO2013/138353 (incorporated by reference) is a comparator compound. Compound No. 1244463 is a 3-9-3 LNA gapmer, having a sequence (from 5' to 3') ATAGGTCCCGCTGCT (SEQ ID NO: 2793), and wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, Compound No. 1244464 ("SH10"), which has been described in WO2013/138353 is a comparator compound. Compound No. 1244464 is a 3-10-3 LNA gapmer, having a sequence (from 5' to 3') TGATAGGTCCCGCTGC (SEQ ID NO: 2794), and wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, Compound No. 1244465 ("SH13"), which has been described in WO2013/138353 is a comparator compound. Compound No. 1244465 is a 3-10-3 LNA gapmer, having a sequence (from 5' to 3') CTGATAGGTCCCGCTG (SEQ ID NO: 2795), and wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, Compound No. 1244466 ("SH16"), which has been described in WO2013/138353 is a comparator compound. Compound No. 1244466 is a 3-9-3 LNA gapmer, having a sequence (from 5' to 3') CTGATAGGTCCCGCT (SEQ ID NO: 2796), and wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

In certain embodiments, Compound No. 1244467 ("SH20"), which has been described in WO2013/138353 is a comparator compound. Compound No. 1244467 is a 2-9-3 LNA gapmer, having a sequence (from 5' to 3') CTGATAGGTCCCGC (SEQ ID NO: 2797), and wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

Compound No. 1244463, Compound No. 1244464, Compound No. 1244465, Compound No. 1244466, and Compound No. 1244467 were selected as comparator compounds because according to Example 2 of WO2013/138353 these compounds were selected for further study. Accordingly, these compounds were tested in further studies.

In certain embodiments, compounds described herein are superior relative to compounds described in Moore, 2017, WO 2018/089805, and WO2013/138353 because they demonstrate one or more improved properties, such as, potency and tolerability.

For example, as described herein, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved an IC_{50} in Example 7, hereinbelow, of 0.10 μM, 0.69 μM, and 0.47 μM, respectively, whereas comparator compound, Compound No. 650528 ("ASO-5") achieved an IC_{50} in Example 7, hereinbelow, of 2.03 μM and Compound No. 650668 ("ASO-2") achieved an IC_{50} in Example 2 of WO 2018/089805 of 1.7 μM. Therefore, certain compounds described herein are more potent than comparator compounds, Compound No. 650528 ("ASO-5") and Compound No. 650668 ("ASO-2") in this assay.

For example, as described herein, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 are more efficacious and potent than comparator compounds *in vivo*. See, e.g., Examples 4, 6,

and 9, hereinbelow. For example, as provided in Examples 4 and 6, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved an average expression level (% control) of 13%, 23%, and 27%, respectively, in spinal cord of transgenic mice whereas comparator compound, Compound No. 650528 ("ASO-5") achieved an average expression level (% control) of 32% in spinal cord of transgenic mice. For example, as provided in Examples 4 and 6, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved an average expression level (% control) of 13%, 23%, and 42%, respectively, in cortex of transgenic mice whereas comparator compound, Compound No. 650528 ("ASO-5") achieved an average expression level (% control) of 43% in cortex of transgenic mice. For example, as provided in Examples 4 and 6, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved an average expression level (% control) of 60%, 62%, and 68%, respectively, in cerebellum of transgenic mice whereas comparator compound, Compound No. 650528 ("ASO-5") achieved an average expression level (% control) of 75% in cerebellum of transgenic mice. For example, as provided in Examples 4 and 6, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved an average expression level (% control) of 14%, 26%, and 23%, respectively, in brain stem of transgenic mice whereas comparator compound, Compound No. 650528 ("ASO-5") achieved an average expression level (% control) of 35% in brain stem of transgenic mice. Therefore, certain compounds described herein are more efficacious than comparator compound, Compound No. 650528 ("ASO-5") in this assay. Specifically, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 are more efficacious than Compound No. 650528 ("ASO-5") in every tissue tested in this assay.

For example, as described herein, certain compounds Compound No. 1100673, Compound No. 1101657, and Compound No. 1102130 achieved 3-hour FOB scores in mice of 1.00 (table 9) and 0.00 (table 20), 1.00 (table 9) and 0.00 (table 20), and 0.00 (table 8 and table 20), respectively, whereas each of comparator compounds Compound No. 1244463, Compound No. 1244464, Compound No. 1244465, Compound No. 1244466, and Compound No. 1244447 achieved 3-hour FOB scores in mice of 7.00 (table 26). Therefore, certain compounds described herein are more tolerable than comparator compounds Compound No. 1244463, Compound No. 1244464, Compound No. 1244465, Compound No. 1244466, and Compound No. 1244447 in this assay.

IX. Certain Hotspot Regions

1. Nucleobases 138-175 of SEQ ID NO: 1

In certain embodiments, nucleobases 138-175 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 138-175 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 1060, 1061, 1062, 1063, 1064, and 1065 are complementary to nucleobases 138-175 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 138-175 of SEQ ID NO: 1 achieve at least 79% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

2. Nucleobases 392-436 of SEQ ID NO: 1

In certain embodiments, nucleobases 392-436 of SEQ ID NO: 1 comprise a hotspot region. In certain

embodiments, modified oligonucleotides are complementary to nucleobases 392-436 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 196, 197, 198 ,199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209 are complementary to nucleobases 392-436 of SEQ ID NO 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 392-436 of SEQ ID NO: 1 achieve an average of 77% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

3. Nucleobases 1120-1146 of SEQ ID NO: 1

In certain embodiments, nucleobases 1120-1146 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 1120-1146 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 313, 314, 315, 316, and 317 are complementary to nucleobases 1120-1146 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 1120-1146 of SEQ ID NO: 1 achieve at least 60% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

4. Nucleobases 1823-1882 of SEQ ID NO:1

In certain embodiments, nucleobases 1823-1882 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 1823-1882 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 413-423 are complementary to nucleobases 1823-1882 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 1823-1882 of SEQ ID NO: 1 achieve at least 60% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

5. Nucleobases 3042-3098 of SEQ ID NO: 1

In certain embodiments, nucleobases 3042-3098 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 3042-3098 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos:43, 44, 45, and 635-653 are complementary to nucleobases 3042-

3098 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 3042-3098 of SEQ ID NO: 1 achieve at least 64% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

6. Nucleobases 3749-3801 of SEQ ID NO: 1

In certain embodiments, nucleobases 3749-3801 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 3749-3801 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 719-732 are complementary to nucleobases 3749-3801 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 3749-3801 of SEQ ID NO: 1 achieve at least 52% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

7. Nucleobases 5997-6021 of SEQ ID NO: 1

In certain embodiments, nucleobases 5997-6021 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 5997-6021 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 920-924 are complementary to nucleobases 5997-6021 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary to nucleobases 5997-6021 of SEQ ID NO: 2 achieve at least 75% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

8. Nucleobases 19437-19476 of SEQ ID NO: 2

In certain embodiments, nucleobases 19437-19476 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 19437-19476 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 1671, 1672, 1673, and 1674 are complementary to nucleobases 19437-19476 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to nucleobases 19437-19476 of SEQ ID NO: 2 achieve at least 83% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

9. Nucleobases 34440-34486 of SEQ ID NO: 2

In certain embodiments, nucleobases 34440-34486 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 34440-34486 of SEQ ID NO: 2. In certain

embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 2233, 2234, 2235, 2236, and 2237 are complementary to nucleobases 34440-34486 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to nucleobases 34440-34486 of SEQ ID NO: 2 achieve at least 71% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

10. Nucleobases 39883-39904 of SEQ ID NO: 2

In certain embodiments, nucleobases 39883-39904 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 39860-39904 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 2510, 2511, and 2512 are complementary to nucleobases 39883-39904 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to nucleobases 39883-39904 of SEQ ID NO: 2 achieve at least 89% reduction of ATXN3 RNA *in vitro* in the standard cell assay.

11. Nucleobases 6597-6618 of SEQ ID NO: 2

In certain embodiments, nucleobases 6597-6618 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 6597-6618 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE. In certain embodiments, the nucleosides of the modified oligonucleotides are linked by phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages.

The nucleobase sequences of SEQ ID Nos: 1226, 1227, and 1228 are complementary to nucleobases 6597-6618 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary to nucleobases 6597-6618 of SEQ ID NO: 2 achieve at least 75% reduction of ATXN3 RNA *in vitro* in the standard cell 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, and the like recited in the present application is incorporated herein by reference in its entirety.

Although the sequence listing accompanying this filing identifies each sequence as either “RNA” or “DNA” as required, in reality, those sequences may be modified with any combination of chemical modifications. One of skill in the art will readily appreciate that such designation as “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 (methylated uracil) in place of a uracil of RNA). Accordingly, nucleic acid sequences provided herein, including, but not limited to those in the sequence listing, are intended to encompass nucleic acids containing any combination of natural or modified RNA and/or DNA, including, but not limited to such nucleic acids having modified nucleobases. By way of further example and without limitation, an oligomeric compound having the nucleobase sequence "ATCGATCG" encompasses any oligomeric compounds having such nucleobase sequence, whether modified or unmodified, including, but not limited to, such compounds comprising RNA bases, such as those having sequence "AUCGAUCG" and those having some DNA bases and some RNA bases such as "AUCGATCG" and oligomeric compounds having other modified nucleobases, such as "AT^{m}CGAUCG," wherein ^{m}C indicates a cytosine base comprising a methyl group at the 5-position.

Certain compounds described herein (e.g., modified oligonucleotides) have one or more asymmetric center and thus give rise to enantiomers, diastereomers, and other stereoisomeric configurations that may be defined, in terms of absolute stereochemistry, as (*R*) or (*S*), as α or β such as for sugar anomers, or as (D) or (L), such as for amino acids, etc. Compounds provided herein that are drawn or described as having certain stereoisomeric configurations include only the indicated compounds. Compounds provided herein that are drawn or described with undefined stereochemistry include all such possible isomers, including their stereorandom and optically pure forms, unless specified otherwise. Likewise, tautomeric forms of the compounds herein are also included unless otherwise indicated. Unless otherwise indicated, compounds described herein are intended to include corresponding salt forms.

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 ^{1}H hydrogen atoms. Isotopic substitutions encompassed by the compounds herein include but are not limited to: ^{2}H or ^{3}H in place of ^{1}H, ^{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: Effect of 5-10-5 MOE gapmers with mixed internucleoside linkages on human ATXN3 *in vitro*, single dose

Modified oligonucleotides complementary to a human ATXN3 nucleic acid were designed and tested for their effect on ATXN3 RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had similar culture conditions.

Cultured A431 cells at a density of 10,000 cells per well were transfected by free uptake with 4,000 nM concentration of modified oligonucleotide or no modified oligonucleotide for untreated controls. After approximately 24 hours, RNA was isolated from the cells and ATXN3 RNA levels were measured by quantitative real-time PCR. Human primer probe set RTS38920 (forward sequence CTATCAGGACAGAGTTCACATCC, designated herein as SEQ ID NO: 6; reverse sequence GTTTCTAAAGACATGGTCACAGC, designated herein as SEQ ID NO: 7; probe sequence AAAGGCCAGCCACCAGTTCAGG, designated herein as SEQ ID: 8) was used to measure RNA levels. ATXN3 RNA levels were adjusted according to total RNA content, as measured by RiboGreen®. Results are presented in the table below as percent ATXN3 RNA levels relative to untreated control cells. The modified oligonucleotides marked with an asterisk (*) target the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of oligonucleotides targeting the amplicon region.

The modified oligonucleotides in the tables below are 5-10-5 MOE gapmers. The gapmers are 20 nucleobases in length, wherein the central gap segment comprises ten 2'-deoxynucleosides and is flanked by wing segments on both the 5' end and on the 3' end comprising five 2'-MOE nucleosides each. The sugar motif for the gapmers is (from 5' to 3'): eeeeddddddddddeeeee; wherein 'd' represents a 2'-deoxyribose sugar and 'e' represents a 2'-MOE modified sugar. All cytosine residues throughout each gapmer are 5-methyl cytosines. The internucleoside linkages are mixed phosphodiester and phosphorothioate linkages. The internucleoside linkage motif for the gapmers is (from 5' to 3'): sooossssssssssooss; wherein 'o' represents a phosphodiester internucleoside linkage and 's' represents a phosphorothioate internucleoside linkage. "Start Site" indicates the 5'-most nucleoside to which the gapmer is complementary in the human nucleic acid sequence. "Stop Site" indicates the 3'-most nucleoside to which the gapmer is complementary in the human nucleic acid sequence.

Each modified oligonucleotide listed in the tables below is complementary to human ATXN3 nucleic acid sequences SEQ ID No: 1, SEQ ID No: 2, SEQ ID No: 3, SEQ ID No: 4, or SEQ ID No: 5, as indicated. 'N/A' indicates that the modified oligonucleotide is not complementary to that particular nucleic acid sequence with 100% complementarity. As shown below, modified oligonucleotides complementary to human ATXN3 reduced the amount of human ATXN3 RNA.

Table 1

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	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')	ATXN3 % control	SEQ ID NO
1100357	15	34	3394	3413	ACCACCCCCTCCAGCTCCGC	88	15
1100359	17	36	3396	3415	GAACCACCCCCTCCAGCTCC	83	16
1100393	383	402	N/A	N/A	TGATCTTTCATTTATAGGAT	86	17

1100395	385	404	N/A	N/A	AATGATCTTTCATTTATAGG	74	18
1100429	458	477	21185	21204	GAGAGAATTCAAGTTAAACC	25	19
1100431	470	489	21197	21216	TGGACCCGTCAAGAGAGAAT	35	20
1100465	638	657	26836	26855	TAATTCTTCTCCAATAAGTT	101	21
1100467	641	660	26839	26858	TGCTAATTCTTCTCCAATAA	92	22
1100501	812	831	27669	27688	CTGAATAGCCCTGCGGAGAT	82	23
1100503	819	838	27676	27695	TACTTAGCTGAATAGCCCTG	99	24
1100573	1222	1241	45748	45767	TGACACATTACCAAAGTGGA	52	25
1100575	1225	1244	45751	45770	CTTTGACACATTACCAAAGT	94	26
1100609	1562	1581	46088	46107	TGGTTAATAAGAAATGAAAG	79	27
1100611	1566	1585	46092	46111	AATTTGGTTAATAAGAAATG	87	28
1100645	1758	1777	46284	46303	AAAAGATTACCATCTTTCAA	64	29
1100647	1760	1779	46286	46305	AGAAAAGATTACCATCTTTC	84	30
1100681	2005	2024	46531	46550	TCCTAGTTTTCTCAATTGGA	94	31
1100683	2007	2026	46533	46552	TCTCCTAGTTTTCTCAATTG	57	32
1100717	2211	2230	46737	46756	CAAGCTATACCTACTAAAAG	76	33
1100719	2213	2232	46739	46758	GACAAGCTATACCTACTAAA	22	34
1100753	2319	2338	46845	46864	CCATTGTTCTTAAGCTATCT	27	35
1100755	2348	2367	46874	46893	ATTTATAGATCCACTAAGTA	85	36
1100789	2540	2559	47066	47085	AGCTTATGAACAATTCAACA	31	37
1100791	2545	2564	47071	47090	ATTTTAGCTTATGAACAATT	78	38
1100825	2659	2678	47185	47204	TTAGCAATAAATCCTAGATC	59	39
1100827	2661	2680	47187	47206	AGTTAGCAATAAATCCTAGA	39	40
1100861	2896	2915	47422	47441	GAGGGAGTAGTACTAAACTC	57	41
1100863	2911	2930	47437	47456	AGCTTTTTAAATCTTGAGGG	21	42
1100897	3042	3061	47568	47587	GCTCATCAATTCAAGTGTAT	31	43
1100899	3044	3063	47570	47589	TAGCTCATCAATTCAAGTGT	31	44
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100934	3539	3558	48065	48084	AAACACATTCAAACGCATCC	69	46
1100936	3541	3560	48067	48086	ACAAACACATTCAAACGCAT	65	47
1100970	3665	3684	48191	48210	TGGCCAATCAATTAAGAAAT	93	48
1100972	3671	3690	48197	48216	TCATACTGGCCAATCAATTA	68	49
1101006	3792	3811	48318	48337	TTAGTTGTTCCTGACTTTCT	59	50
1101008	3803	3822	48329	48348	TTCTTGTGAATTTAGTTGTT	43	51
1101042	3918	3937	48444	48463	GTAATACAAATTATACATTA	104	52
1101044	3921	3940	48447	48466	CCAGTAATACAAATTATACA	53	53
1101078	4010	4029	48536	48555	ACTCATTAAATCCATGACAT	53	54
1101080	4012	4031	48538	48557	TTACTCATTAAATCCATGAC	62	55
1101114	4123	4142	48649	48668	CAGCCTTTTCAAACAGTTTA	39	56
1101116	4125	4144	48651	48670	AGCAGCCTTTTCAAACAGTT	31	57
1101150	4402	4421	48928	48947	TAGTATCAAAAATTCAGACA	90	58
1101152	4757	4776	49283	49302	GTTTTAAGAATTTAGTAGCT	71	59

1101186	5957	5976	50483	50502	TCGATACAACAAACAATTCA	62	60
1101188	5959	5978	50485	50504	ACTCGATACAACAAACAATT	80	61
1101222	6143	6162	50669	50688	GACTAAAAAAATACAAAGCC	78	62
1101224	6200	6219	50726	50745	TCAATAATCTTCACTCATGA	87	63
1101258	6539	6558	51065	51084	ACATTTAAAAATGTATGTTT	83	64
1101260	6551	6570	51077	51096	AATTAGATAATCACATTTAA	102	65
1101294	6660	6679	51186	51205	GCCAAACAACAATGCTTTTT	58	66
1101296	6662	6681	51188	51207	TGGCCAAACAACAATGCTTT	93	67
1101330	6882	6901	51408	51427	ATTTAATAATCTTTGATATT	76	68
1101332	6890	6909	51416	51435	TTATCTTTATTTAATAATCT	87	69
1101366	207	226	13276	13295	CTCCTCCTTCTGCCATTCTC	57	70
1101368	212	231	13281	13300	AGTAACTCCTCCTTCTGCCA	43	71
1101438	N/A	N/A	53335	53354	CTACCCTAATACAAGAGACT	108	72
1101440	N/A	N/A	53468	53487	AAACCCTACAAATACTGAAT	102	73
1101582	N/A	N/A	4112	4131	AACCAAACCCAAACATCCCG	59	74
1101584	N/A	N/A	4114	4133	GAAACCAAACCCAAACATCC	87	75
1101618	N/A	N/A	4906	4925	TCAGCCTATTTCAAAAGTTT	100	76
1101620	N/A	N/A	4954	4973	AAAATTAGTGACAACTATAC	78	77
1101654	N/A	N/A	6579	6598	AAACTCAAAGCCATCTCTTT	80	78
1101656	N/A	N/A	6594	6613	CCATATATATCTCAGAAACT	84	79
1101690	N/A	N/A	7113	7132	AAGTCATTTATACAGAATTT	69	80
1101692	N/A	N/A	7146	7165	CAGAGGTTTCAAAACCTGTG	73	81
1101726	N/A	N/A	8509	8528	TTATCTCAAACTATCCCCAG	91	82
1101728	N/A	N/A	8512	8531	CCCTTATCTCAAACTATCCC	99	83
1101762	N/A	N/A	9034	9053	AGTTTACAAACTATGGTCAC	79	84
1101764	N/A	N/A	9037	9056	TGGAGTTTACAAACTATGGT	37	85
1101798	N/A	N/A	9800	9819	TAACCAATAATAACTAATAA	87	86
1101800	N/A	N/A	9807	9826	ATTGGTATAACCAATAATAA	110	87
1101834	N/A	N/A	11212	11231	CTGTCCCAAACAACCCTGGA	88	88
1101836	N/A	N/A	11217	11236	CAGAACTGTCCCAAACAACC	85	89
1101870	N/A	N/A	12035	12054	TTACATGATCAAAAATTTAA	85	90
1101872	N/A	N/A	12070	12089	TTTATTTTACAAATCTACCA	88	91
1101906	N/A	N/A	14226	14245	ACGGTGAAACCCCACTATCT	79	92
1101908	N/A	N/A	14332	14351	CTATATAAAAATCTAGTACT	102	93
1101942	N/A	N/A	15045	15064	ATAAACAAAGATATCTGCAG	98	94
1101944	N/A	N/A	15201	15220	AGCAAGGCACAAATAGGAAA	95	95
1101978	N/A	N/A	15710	15729	ATATATCACTAAATCCATAA	75	96
1101980	N/A	N/A	15713	15732	TAGATATATCACTAAATCCA	77	97
1102014	N/A	N/A	16642	16661	ATTAACTTGAAATATTGAAT	110	98
1102016	N/A	N/A	16674	16693	ATCTTTCATTTCTAAAAAAG	83	99
1102050	N/A	N/A	17448	17467	TGACACTATTTCAGGCTTTG	7	100
1102052	N/A	N/A	17466	17485	GAATGCTTTATTCATGCTTG	31	101
1102086	N/A	N/A	18832	18851	TAAGAAAGAACCAACTTAGG	85	102

1102088	N/A	N/A	18841	18860	GAAGAACTTTAAGAAAGAAC	83	103
1102122	N/A	N/A	19392	19411	TAGTGAAAAATATAGTTTTA	112	104
1102124	N/A	N/A	19394	19413	TATAGTGAAAAATATAGTTT	90	105
1102158	N/A	N/A	19863	19882	ACATTTTTTTAAAAGAGATG	108	106
1102160	N/A	N/A	19882	19901	TCACATATAACATATAAACA	75	107
1102194	N/A	N/A	20985	21004	CTGCAGATTTATCACTATTA	71	108
1102196	N/A	N/A	21009	21028	GATCTTAAAAACTACAAGAG	69	109
1102230	N/A	N/A	22011	22030	CGAGTCAGATCCTAAAATCA	77	110
1102232	N/A	N/A	22184	22203	GGTGGTAGTTAAAGAGTAAT	74	111
1102266	N/A	N/A	22927	22946	TAACGGAAAGCCACAAGGAA	103	112
1102268	N/A	N/A	22966	22985	GAACATAATTTTAATTGCTT	65	113
1102302	N/A	N/A	23986	24005	GTATCTAAAATCAAAGAATT	81	114
1102304	N/A	N/A	23989	24008	CAAGTATCTAAAATCAAAGA	89	115
1102338	N/A	N/A	25018	25037	ATGGAAAACCTCAAAATAGT	81	116
1102340	N/A	N/A	25428	25447	TTTAAGTTTCTCTATCATTA	87	117
1102374	N/A	N/A	25709	25728	GTGTGCAATAACTAGTAACA	33	118
1102376	N/A	N/A	25807	25826	TACATTACCCTTCATATATA	77	119
1102410	N/A	N/A	26869	26888	GCCTCATTTTTACCTTTGCT	64	120
1102412	N/A	N/A	26871	26890	AGGCCTCATTTTTACCTTTG	104	121
1102446	N/A	N/A	27823	27842	AAGGGAAAGCCCACTATATA	90	122
1102448	N/A	N/A	27834	27853	TAAGAAATCTAAAGGGAAAG	93	123
1102482	N/A	N/A	28191	28210	TTAACATTTTTCTTTGCCTA	76	124
1102484	N/A	N/A	28228	28247	ACTTCAAACTTTTAATTAAG	86	125
1102518	N/A	N/A	28890	28909	AATCACTGTATTTACCAATT	99	126
1102520	N/A	N/A	28901	28920	CAACAAAAACCAATCACTGT	98	127
1102554	N/A	N/A	29810	29829	GAGTTGATCCAGATTTATGG	41	128
1102556	N/A	N/A	29863	29882	GGAATTCCTATTTAGCAAGC	78	129
1102590	N/A	N/A	30581	30600	TAGAAATATCTCACATTAAG	70	130
1102592	N/A	N/A	30586	30605	AAGACTAGAAATATCTCACA	56	131
1102626	N/A	N/A	31259	31278	TGATTATTATTTTATGACAA	75	132
1102628	N/A	N/A	31312	31331	TATTTTTTACATTAACTAGA	79	133
1102662	N/A	N/A	33021	33040	TCTGAAATAAACATGGTGAA	72	134
1102664	N/A	N/A	33385	33404	TTATAGTTTCTCTATGATGT	69	135
1102698	N/A	N/A	34137	34156	AAGAAGTTAGTTCTTAACTC	72	136
1102700	N/A	N/A	34168	34187	TGAATGCAAGCCATTGTTAA	52	137
1102734	N/A	N/A	34497	34516	GCATGAAAACTATGATTACT	18	138
1102736	N/A	N/A	34499	34518	ATGCATGAAAACTATGATTA	69	139
1102770	N/A	N/A	35322	35341	TTATGTAAACCCCTAATTTC	109	140
1102772	N/A	N/A	35438	35457	TAATATCCTCATTACCCATT	89	141
1102806	N/A	N/A	36969	36988	TTAGCAAATCCTGATGCTGC	72	142
1102808	N/A	N/A	36980	36999	GTATCCTCCCATTAGCAAAT	35	143
1102842	N/A	N/A	37709	37728	TATTATTCCCAAATGGTTCA	64	144
1102844	N/A	N/A	37730	37749	TAATGGAAAATCATATCTGC	56	145

1102878	N/A	N/A	38268	38287	CCTTTGATCAGATAAAGCAT	62	146
1102880	N/A	N/A	38289	38308	GAAAGTCACCAAAAATAAGT	75	147
1102914	N/A	N/A	38842	38861	ACATTGTTTCACGAATCAAA	65	148
1102916	N/A	N/A	38853	38872	ATAAGGAAAATACATTGTTT	111	149
1100537*	1088	1107	45614	45633	CATGGTCACAGCTGCCTGAA	31	150
1100539*	1090	1109	45616	45635	GACATGGTCACAGCTGCCTG	16	151
1102950*	N/A	N/A	39345	39364	TGAAGTTTAAATTATTATGT	79	152
1102952*	N/A	N/A	39361	39380	ACTGTACAAATTACTGTGAA	67	153
1102986*	N/A	N/A	40095	40114	TTATTTCTTCATTAAAGCCA	50	154
1102988*	N/A	N/A	40202	40221	CAAAAAAATGCCAAACTGTT	96	155
1103022*	N/A	N/A	42830	42849	GCTGTCATTCAAATTGCTTA	60	156
1103024*	N/A	N/A	42892	42911	ACTAGAAAAAATGTTGTATG	74	157
1103058*	N/A	N/A	44033	44052	TAAAATAGTTTTCTAAATGT	108	158
1103060*	N/A	N/A	44071	44090	AATATTAGCCAAAGAGGCAT	106	159
1103094*	N/A	N/A	45111	45130	TGTAAAGATATTTAAGAGAG	75	160
1103096*	N/A	N/A	45130	45149	CTGTCAATTCAAAGGAAGTT	51	161

Table 2

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	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')	ATXN3 (% control)	SEQ ID NO
1100358	16	35	3395	3414	AACCACCCCCTCCAGCTCCG	85	162
1100360	18	37	3397	3416	CGAACCACCCCCTCCAGCTC	111	163
1100361	19	38	3398	3417	CCGAACCACCCCCTCCAGCT	103	164
1100362	44	63	3423	3442	TTGTCTGGAGCCAACGGCCC	64	165
1100363	56	75	3435	3454	CTCCATGTTTATTTGTCTGG	97	166
1100364	57	76	3436	3455	ACTCCATGTTTATTTGTCTG	86	167
1100365	63	82	3442	3461	AGATGGACTCCATGTTTATT	89	168
1100368	312	331	16178	16197	CCCAAACTTTCAAGGCATTG	79	169
1100369	313	332	16179	16198	CCCCAAACTTTCAAGGCATT	30	170
1100370	314	333	16180	16199	ACCCCAAACTTTCAAGGCAT	36	171
1100371	315	334	16181	16200	AACCCCAAACTTTCAAGGCA	50	172
1100372	316	335	16182	16201	AAACCCCAAACTTTCAAGGC	45	173
1100373	319	338	16185	16204	TCTAAACCCCAAACTTTCAA	57	174
1100374	320	339	16186	16205	TTCTAAACCCCAAACTTTCA	92	175
1100375	321	340	16187	16206	GTTCTAAACCCCAAACTTTC	48	176
1100376	322	341	16188	16207	AGTTCTAAACCCCAAACTTT	63	177
1100377	323	342	16189	16208	TAGTTCTAAACCCCAAACTT	81	178
1100378	324	343	16190	16209	TTAGTTCTAAACCCCAAACT	58	179
1100379	326	345	16192	16211	GATTAGTTCTAAACCCCAAA	15	180

1100380	327	346	16193	16212	GGATTAGTTCTAAACCCCAA	25	181
1100381	328	347	16194	16213	AGGATTAGTTCTAAACCCCA	23	182
1100382	330	349	16196	16215	ACAGGATTAGTTCTAAACCC	24	183
1100383	338	357	16204	16223	ACTGTTGAACAGGATTAGTT	64	184
1100384	356	375	16222	16241	GAGCCTCTGATACTCTGGAC	23	185
1100385	357	376	16223	16242	TGAGCCTCTGATACTCTGGA	51	186
1100386	359	378	16225	16244	CCTGAGCCTCTGATACTCTG	88	187
1100387	363	382	16229	16248	CGATCCTGAGCCTCTGATAC	41	188
1100388	368	387	16234	16253	AGGATCGATCCTGAGCCTCT	78	189
1100389	369	388	16235	16254	TAGGATCGATCCTGAGCCTC	91	190
1100390	371	390	N/A	N/A	TATAGGATCGATCCTGAGCC	60	191
1100391	372	391	N/A	N/A	TTATAGGATCGATCCTGAGC	71	192
1100392	381	400	N/A	N/A	ATCTTTCATTTATAGGATCG	59	193
1100394	384	403	N/A	N/A	ATGATCTTTCATTTATAGGA	92	194
1100396	391	410	16684	16703	CATATAAATGATCTTTCATT	79	195
1100397	392	411	16685	16704	GCATATAAATGATCTTTCAT	7	196
1100398	393	412	16686	16705	TGCATATAAATGATCTTTCA	12	197
1100399	394	413	16687	16706	TTGCATATAAATGATCTTTC	13	198
1100400	395	414	16688	16707	ATTGCATATAAATGATCTTT	31	199
1100401	397	416	16690	16709	TAATTGCATATAAATGATCT	68	200
1100402	403	422	16696	16715	TCCTTATAATTGCATATAAA	35	201
1100403	406	425	16699	16718	TGTTCCTTATAATTGCATAT	15	202
1100404	407	426	16700	16719	GTGTTCCTTATAATTGCATA	76	203
1100405	408	427	16701	16720	AGTGTTCCTTATAATTGCAT	7	204
1100406	409	428	16702	16721	CAGTGTTCCTTATAATTGCA	7	205
1100407	410	429	16703	16722	CCAGTGTTCCTTATAATTGC	10	206
1100408	411	430	16704	16723	ACCAGTGTTCCTTATAATTG	7	207
1100409	412	431	16705	16724	AACCAGTGTTCCTTATAATT	12	208
1100410	417	436	16710	16729	CTGTAAACCAGTGTTCCTTA	19	209
1100411	420	439	16713	16732	TAACTGTAAACCAGTGTTCC	80	210
1100412	421	440	16714	16733	CTAACTGTAAACCAGTGTTC	32	211
1100413	427	446	16720	16739	AATTTTCTAACTGTAAACCA	86	212
1100414	430	449	16723	16742	CCTAATTTTCTAACTGTAAA	79	213
1100415	431	450	16724	16743	TCCTAATTTTCTAACTGTAA	81	214
1100416	432	451	16725	16744	TTCCTAATTTTCTAACTGTA	71	215
1100417	433	452	16726	16745	TTTCCTAATTTTCTAACTGT	68	216
1100418	435	454	16728	16747	GTTTTCCTAATTTTCTAACT	75	217
1100419	438	457	N/A	N/A	ACTGTTTTCCTAATTTTCTA	56	218
1100420	440	459	N/A	N/A	CCACTGTTTTCCTAATTTTC	46	219
1100421	441	460	N/A	N/A	ACCACTGTTTTCCTAATTTT	38	220
1100422	442	461	N/A	N/A	AACCACTGTTTTCCTAATTT	48	221
1100423	447	466	N/A	N/A	AGTTAAACCACTGTTTTCCT	49	222
1100424	448	467	N/A	N/A	AAGTTAAACCACTGTTTTCC	58	223

1100425	450	469	N/A	N/A	TCAAGTTAAACCACTGTTTT	60	224
1100426	451	470	N/A	N/A	TTCAAGTTAAACCACTGTTT	60	225
1100427	453	472	N/A	N/A	AATTCAAGTTAAACCACTGT	66	226
1100428	456	475	21183	21202	GAGAATTCAAGTTAAACCAC	37	227
1100430	463	482	21190	21209	GTCAAGAGAGAATTCAAGTT	22	228
1100432	472	491	21199	21218	TCTGGACCCGTCAAGAGAGA	40	229
1100433	493	512	21220	21239	AGATATGTATCTGATATTAA	47	230
1100434	500	519	21227	21246	AAGTGCAAGATATGTATCTG	20	231
1100435	501	520	21228	21247	AAAGTGCAAGATATGTATCT	34	232
1100436	502	521	21229	21248	AAAAGTGCAAGATATGTATC	51	233
1100437	507	526	21234	21253	CCAAGAAAAGTGCAAGATAT	45	234
1100438	511	530	21238	21257	TGAGCCAAGAAAAGTGCAAG	77	235
1100439	512	531	21239	21258	TTGAGCCAAGAAAAGTGCAA	78	236
1100440	515	534	21242	21261	TAATTGAGCCAAGAAAAGTG	75	237
1100441	517	536	21244	21263	TGTAATTGAGCCAAGAAAAG	77	238
1100442	522	541	21249	21268	CCTGTTGTAATTGAGCCAAG	42	239
1100443	531	550	N/A	N/A	AATAACCTTCCTGTTGTAAT	61	240
1100444	532	551	N/A	N/A	GAATAACCTTCCTGTTGTAA	54	241
1100445	533	552	N/A	N/A	AGAATAACCTTCCTGTTGTA	47	242
1100446	534	553	N/A	N/A	TAGAATAACCTTCCTGTTGT	51	243
1100447	535	554	N/A	N/A	ATAGAATAACCTTCCTGTTG	62	244
1100448	536	555	N/A	N/A	TATAGAATAACCTTCCTGTT	64	245
1100449	537	556	N/A	N/A	ATATAGAATAACCTTCCTGT	80	246
1100450	539	558	N/A	N/A	AAATATAGAATAACCTTCCT	73	247
1100451	540	559	N/A	N/A	CAAATATAGAATAACCTTCC	73	248
1100452	541	560	N/A	N/A	ACAAATATAGAATAACCTTC	76	249
1100453	546	565	26744	26763	TAACGACAAATATAGAATAA	93	250
1100454	558	577	26756	26775	GCAGATCACCCTTAACGACA	26	251
1100455	561	580	26759	26778	CTGGCAGATCACCCTTAACG	35	252
1100456	563	582	26761	26780	ATCTGGCAGATCACCCTTAA	54	253
1100457	564	583	26762	26781	AATCTGGCAGATCACCCTTA	75	254
1100458	565	584	26763	26782	CAATCTGGCAGATCACCCTT	49	255
1100459	566	585	26764	26783	GCAATCTGGCAGATCACCCT	48	256
1100460	567	586	26765	26784	CGCAATCTGGCAGATCACCC	60	257
1100461	568	587	26766	26785	TCGCAATCTGGCAGATCACC	48	258
1100462	569	588	26767	26786	TTCGCAATCTGGCAGATCAC	87	259
1100463	571	590	26769	26788	GCTTCGCAATCTGGCAGATC	67	260
1100464	635	654	26833	26852	TTCTTCTCCAATAAGTTTTG	81	261
1100466	639	658	26837	26856	CTAATTCTTCTCCAATAAGT	96	262
1100468	642	661	26840	26859	GTGCTAATTCTTCTCCAATA	23	263
1100469	644	663	26842	26861	TTGTGCTAATTCTTCTCCAA	72	264
1100470	645	664	26843	26862	GTTGTGCTAATTCTTCTCCA	34	265
1100471	675	694	N/A	N/A	GGTCTGTTTTATGGACTCTT	60	266

1100472	677	696	27534	27553	CAGGTCTGTTTTATGGACTC	86	267
1100473	678	697	27535	27554	CCAGGTCTGTTTTATGGACT	69	268
1100474	700	719	27557	27576	TCATTTGCTTCTAACACTCG	87	269
1100475	705	724	27562	27581	AGCCATCATTTGCTTCTAAC	19	270
1100476	711	730	27568	27587	TTCCTGAGCCATCATTTGCT	80	271
1100477	712	731	27569	27588	ATTCCTGAGCCATCATTTGC	52	272
1100478	713	732	27570	27589	CATTCCTGAGCCATCATTTG	56	273
1100479	718	737	27575	27594	TCTAACATTCCTGAGCCATC	18	274
1100480	739	758	27596	27615	TGCAAATCCTCCTCATCTTC	42	275
1100481	740	759	27597	27616	CTGCAAATCCTCCTCATCTT	53	276
1100482	741	760	27598	27617	TCTGCAAATCCTCCTCATCT	53	277
1100483	742	761	27599	27618	CTCTGCAAATCCTCCTCATC	64	278
1100484	743	762	27600	27619	CCTCTGCAAATCCTCCTCAT	46	279
1100485	745	764	27602	27621	GCCCTCTGCAAATCCTCCTC	58	280
1100486	752	771	27609	27628	TGCCAGAGCCCTCTGCAAAT	68	281
1100487	754	773	27611	27630	AGTGCCAGAGCCCTCTGCAA	64	282
1100488	760	779	27617	27636	CGACTTAGTGCCAGAGCCCT	86	283
1100489	762	781	27619	27638	GGCGACTTAGTGCCAGAGCC	83	284
1100490	767	786	27624	27643	TTCTTGGCGACTTAGTGCCA	59	285
1100491	776	795	27633	27652	CATGTCAATTTCTTGGCGAC	83	286
1100492	777	796	27634	27653	CCATGTCAATTTCTTGGCGA	72	287
1100493	786	805	27643	27662	CCTCATCTTCCATGTCAATT	66	288
1100494	788	807	27645	27664	TTCCTCATCTTCCATGTCAA	52	289
1100495	789	808	27646	27665	CTTCCTCATCTTCCATGTCA	47	290
1100496	792	811	27649	27668	CTGCTTCCTCATCTTCCATG	28	291
1100497	793	812	27650	27669	TCTGCTTCCTCATCTTCCAT	33	292
1100498	794	813	27651	27670	ATCTGCTTCCTCATCTTCCA	37	293
1100499	795	814	27652	27671	GATCTGCTTCCTCATCTTCC	43	294
1100500	796	815	27653	27672	AGATCTGCTTCCTCATCTTC	45	295
1100502	814	833	27671	27690	AGCTGAATAGCCCTGCGGAG	68	296
1100504	827	846	27684	27703	ACCTTGCATACTTAGCTGAA	77	297
1100505	833	852	N/A	N/A	GGAACTACCTTGCATACTTA	20	298
1100506	836	855	N/A	N/A	TCTGGAACTACCTTGCATAC	47	299
1100507	838	857	N/A	N/A	TTTCTGGAACTACCTTGCAT	69	300
1100508	875	894	28970	28989	ATTTGTACCTGATGTCTGTG	30	301
1100509	877	896	28972	28991	AGATTTGTACCTGATGTCTG	50	302
1100510	883	902	28978	28997	GAAGTAAGATTTGTACCTGA	41	303
1100511	885	904	28980	28999	CTGAAGTAAGATTTGTACCT	91	304
1100512	886	905	28981	29000	TCTGAAGTAAGATTTGTACC	91	305
1100513	904	923	28999	29018	CGTCTCTTCCGAAGCTCTTC	69	306
1100514	926	945	N/A	N/A	CTGTTTTTCAAAGTAGGCTT	41	307
1100515	927	946	N/A	N/A	GCTGTTTTTCAAAGTAGGCT	67	308
1100516	928	947	N/A	N/A	TGCTGTTTTTCAAAGTAGGC	43	309

1100517	929	948	N/A	N/A	CTGCTGTTTTTCAAAGTAGG	81	310
1100518	930	949	N/A	N/A	GCTGCTGTTTTTCAAAGTAG	65	311
1100519	931	950	N/A	N/A	TGCTGCTGTTTTTCAAAGTA	44	312
1100557	1120	1139	45646	45665	GTTTTCAAATCATTTCTGAC	19	313
1100558	1121	1140	45647	45666	TGTTTTCAAATCATTTCTGA	40	314
1100559	1122	1141	45648	45667	CTGTTTTCAAATCATTTCTG	12	315
1100560	1126	1145	45652	45671	CCTTCTGTTTTCAAATCATT	20	316
1100561	1127	1146	45653	45672	TCCTTCTGTTTTCAAATCAT	20	317
1100562	1143	1162	45669	45688	AAAGGTATTATTTTTTTCCT	39	318
1100563	1144	1163	45670	45689	TAAAGGTATTATTTTTTTCC	29	319
1100564	1145	1164	45671	45690	TTAAAGGTATTATTTTTTTC	122	320
1100565	1167	1186	45693	45712	GTATGAATATCTAAATTATT	80	321
1100566	1172	1191	45698	45717	GGAAAGTATGAATATCTAAA	3	322
1100567	1176	1195	45702	45721	TGTTGGAAAGTATGAATATC	19	323
1100568	1209	1228	45735	45754	AAGTGGACCCTATGCTGTAA	20	324
1100569	1210	1229	45736	45755	AAAGTGGACCCTATGCTGTA	50	325
1100570	1211	1230	45737	45756	CAAAGTGGACCCTATGCTGT	85	326
1100571	1220	1239	45746	45765	ACACATTACCAAAGTGGACC	14	327
1100572	1221	1240	45747	45766	GACACATTACCAAAGTGGAC	13	328
1100574	1223	1242	45749	45768	TTGACACATTACCAAAGTGG	25	329
1100576	1226	1245	45752	45771	TCTTTGACACATTACCAAAG	64	330
1100577	1227	1246	45753	45772	CTCTTTGACACATTACCAAA	35	331
1100578	1228	1247	45754	45773	TCTCTTTGACACATTACCAA	54	332
1100579	1230	1249	45756	45775	CATCTCTTTGACACATTACC	34	333
1100580	1232	1251	45758	45777	CTCATCTCTTTGACACATTA	16	334
1100581	1235	1254	45761	45780	TTCCTCATCTCTTTGACACA	33	335
1100582	1240	1259	45766	45785	CTTATTTCCTCATCTCTTTG	33	336
1100583	1243	1262	45769	45788	AGTCTTATTTCCTCATCTCT	17	337
1100584	1244	1263	45770	45789	AAGTCTTATTTCCTCATCTC	81	338
1100585	1245	1264	45771	45790	AAAGTCTTATTTCCTCATCT	10	339
1100586	1246	1265	45772	45791	AAAAGTCTTATTTCCTCATC	31	340
1100587	1307	1326	45833	45852	TTATTTAGTCCTACAACCGA	62	341
1100588	1311	1330	45837	45856	ATCATTATTTAGTCCTACAA	30	342
1100589	1314	1333	45840	45859	AAGATCATTATTTAGTCCTA	17	343
1100590	1317	1336	45843	45862	TGGAAGATCATTATTTAGTC	6	344
1100591	1318	1337	45844	45863	TTGGAAGATCATTATTTAGT	11	345
1100592	1319	1338	45845	45864	TTTGGAAGATCATTATTTAG	23	346
1100593	1321	1340	45847	45866	TATTTGGAAGATCATTATTT	66	347
1100594	1322	1341	45848	45867	ATATTTGGAAGATCATTATT	84	348
1100595	1331	1350	45857	45876	CTTTGGCTAATATTTGGAAG	37	349
1100596	1332	1351	45858	45877	TCTTTGGCTAATATTTGGAA	43	350
1100597	1333	1352	45859	45878	CTCTTTGGCTAATATTTGGA	12	351
1100598	1344	1363	45870	45889	TTGCTGAATGCCTCTTTGGC	33	352

1100599	1400	1419	45926	45945	TTGCACACTCAAAAAAGAAA	72	353
1100600	1402	1421	45928	45947	TATTGCACACTCAAAAAAGA	105	354
1100601	1403	1422	45929	45948	ATATTGCACACTCAAAAAAG	70	355
1100602	1441	1460	45967	45986	AAGATCCAAGAAAAATGCCC	78	356
1100603	1447	1466	45973	45992	TGCAAAAAGATCCAAGAAAA	105	357
1100604	1448	1467	45974	45993	CTGCAAAAAGATCCAAGAAA	65	358
1100605	1449	1468	45975	45994	TCTGCAAAAAGATCCAAGAA	68	359
1100606	1498	1517	46024	46043	AGAAAACAAACTATATGGAA	87	360
1100607	1550	1569	46076	46095	AATGAAAGCCACTATTACAT	74	361
1100608	1552	1571	46078	46097	GAAATGAAAGCCACTATTAC	59	362
1100610	1565	1584	46091	46110	ATTTGGTTAATAAGAAATGA	103	363
1100612	1567	1586	46093	46112	TAATTTGGTTAATAAGAAAT	87	364
1100613	1575	1594	46101	46120	TGAAAGGTTAATTTGGTTAA	93	365
1100614	1576	1595	46102	46121	CTGAAAGGTTAATTTGGTTA	70	366
1100615	1583	1602	46109	46128	TACTTTCCTGAAAGGTTAAT	109	367
1100616	1586	1605	46112	46131	AGATACTTTCCTGAAAGGTT	72	368
1100617	1587	1606	46113	46132	GAGATACTTTCCTGAAAGGT	97	369
1100618	1588	1607	46114	46133	AGAGATACTTTCCTGAAAGG	107	370
1100619	1611	1630	46137	46156	ACTATTATCAACATCAGGAA	90	371
1100620	1619	1638	46145	46164	GAACCATTACTATTATCAAC	120	372
1100621	1620	1639	46146	46165	AGAACCATTACTATTATCAA	31	373
1100622	1621	1640	46147	46166	TAGAACCATTACTATTATCA	31	374
1100623	1623	1642	46149	46168	TCTAGAACCATTACTATTAT	81	375
1100624	1624	1643	46150	46169	TTCTAGAACCATTACTATTA	60	376
1100625	1625	1644	46151	46170	CTTCTAGAACCATTACTATT	78	377
1100626	1626	1645	46152	46171	CCTTCTAGAACCATTACTAT	46	378
1100627	1627	1646	46153	46172	TCCTTCTAGAACCATTACTA	60	379
1100628	1679	1698	46205	46224	ACACAAGAAAACACTGGAGC	36	380
1100629	1681	1700	46207	46226	CAACACAAGAAAACACTGGA	72	381
1100630	1691	1710	46217	46236	TCAGAGAAAACAACACAAGA	70	382
1100631	1721	1740	46247	46266	AATGAAAACCAGGTAGCAGA	64	383
1100632	1723	1742	46249	46268	ATAATGAAAACCAGGTAGCA	77	384
1100633	1727	1746	46253	46272	GAAAATAATGAAAACCAGGT	63	385
1100634	1731	1750	46257	46276	GTGGGAAAATAATGAAAACC	35	386
1100635	1732	1751	46258	46277	TGTGGGAAAATAATGAAAAC	73	387
1100636	1733	1752	46259	46278	TTGTGGGAAAATAATGAAAA	71	388
1100637	1743	1762	46269	46288	TTCAAAAGAATTGTGGGAAA	81	389
1100638	1745	1764	46271	46290	CTTTCAAAAGAATTGTGGGA	44	390
1100639	1746	1765	46272	46291	TCTTTCAAAAGAATTGTGGG	42	391
1100640	1748	1767	46274	46293	CATCTTTCAAAAGAATTGTG	66	392
1100641	1749	1768	46275	46294	CCATCTTTCAAAAGAATTGT	26	393
1100642	1750	1769	46276	46295	ACCATCTTTCAAAAGAATTG	52	394
1100643	1754	1773	46280	46299	GATTACCATCTTTCAAAAGA	44	395

1100644	1757	1776	46283	46302	AAAGATTACCATCTTTCAAA	96	396
1100646	1759	1778	46285	46304	GAAAAGATTACCATCTTTCA	39	397
1100648	1761	1780	46287	46306	CAGAAAAGATTACCATCTTT	91	398
1100649	1762	1781	46288	46307	TCAGAAAAGATTACCATCTT	66	399
1100650	1763	1782	46289	46308	CTCAGAAAAGATTACCATCT	67	400
1100651	1764	1783	46290	46309	CCTCAGAAAAGATTACCATC	62	401
1100652	1772	1791	46298	46317	ACGCTAAACCTCAGAAAAGA	67	402
1100653	1804	1823	46330	46349	CATGAAATAATGATCCCATC	98	403
1100654	1805	1824	46331	46350	TCATGAAATAATGATCCCAT	60	404
1100655	1806	1825	46332	46351	GTCATGAAATAATGATCCCA	44	405
1100656	1807	1826	46333	46352	AGTCATGAAATAATGATCCC	94	406
1100657	1808	1827	46334	46353	CAGTCATGAAATAATGATCC	68	407
1100658	1809	1828	46335	46354	CCAGTCATGAAATAATGATC	54	408
1100659	1810	1829	46336	46355	ACCAGTCATGAAATAATGAT	80	409
1100660	1819	1838	46345	46364	TAGGAACGCACCAGTCATGA	38	410
1100661	1821	1840	46347	46366	TTTAGGAACGCACCAGTCAT	50	411
1100662	1822	1841	46348	46367	GTTTAGGAACGCACCAGTCA	55	412
1100663	1823	1842	46349	46368	AGTTTAGGAACGCACCAGTC	35	413
1100664	1824	1843	46350	46369	GAGTTTAGGAACGCACCAGT	31	414
1100665	1825	1844	46351	46370	AGAGTTTAGGAACGCACCAG	22	415
1100666	1826	1845	46352	46371	CAGAGTTTAGGAACGCACCA	16	416
1100667	1827	1846	46353	46372	TCAGAGTTTAGGAACGCACC	13	417
1100668	1829	1848	46355	46374	TTTCAGAGTTTAGGAACGCA	16	418
1100669	1835	1854	46361	46380	GGCTGATTTCAGAGTTTAGG	12	419
1100670	1860	1879	46386	46405	CATTTATTCTCAAGTACTTG	25	420
1100671	1861	1880	46387	46406	TCATTTATTCTCAAGTACTT	40	421
1100672	1862	1881	46388	46407	CTCATTTATTCTCAAGTACT	31	422
1100673	1863	1882	46389	46408	GCTCATTTATTCTCAAGTAC	12	423
1100674	1868	1887	46394	46413	AAAATGCTCATTTATTCTCA	49	424
1100675	1889	1908	46415	46434	GCACATGCTCACACATTTTA	43	425
1100676	1927	1946	46453	46472	GATATAAGTGAAAAGACATT	80	426
1100677	1953	1972	46479	46498	GGGTTGCAACAAAGCTGTAA	40	427
1100678	1980	1999	46506	46525	AAGGAAAAAATAAGGCGCAG	71	428
1100679	1982	2001	46508	46527	GAAAGGAAAAAATAAGGCGC	97	429
1100680	2004	2023	46530	46549	CCTAGTTTTCTCAATTGGAG	98	430
1100682	2006	2025	46532	46551	CTCCTAGTTTTCTCAATTGG	53	431
1100684	2009	2028	46535	46554	CTTCTCCTAGTTTTCTCAAT	45	432
1100685	2014	2033	46540	46559	CTATGCTTCTCCTAGTTTTC	50	433
1100686	2015	2034	46541	46560	ACTATGCTTCTCCTAGTTTT	61	434
1100687	2023	2042	46549	46568	GCCTGCATACTATGCTTCTC	68	435
1100688	2024	2043	46550	46569	TGCCTGCATACTATGCTTCT	92	436
1100689	2030	2049	46556	46575	GAGACTTGCCTGCATACTAT	33	437
1100690	2045	2064	46571	46590	GTCTTCTAACAGAAGGAGAC	125	438

1100691	2046	2065	46572	46591	AGTCTTCTAACAGAAGGAGA	137	439
1100692	2047	2066	46573	46592	TAGTCTTCTAACAGAAGGAG	72	440
1100693	2048	2067	46574	46593	TTAGTCTTCTAACAGAAGGA	81	441
1100694	2049	2068	46575	46594	TTTAGTCTTCTAACAGAAGG	85	442
1100695	2050	2069	46576	46595	GTTTAGTCTTCTAACAGAAG	42	443
1100696	2052	2071	46578	46597	ATGTTTAGTCTTCTAACAGA	43	444
1100697	2054	2073	46580	46599	GTATGTTTAGTCTTCTAACA	19	445
1100698	2091	2110	46617	46636	GGCCAAATTTCATGTATCAT	35	446
1100699	2093	2112	46619	46638	AAGGCCAAATTTCATGTATC	48	447
1100700	2094	2113	46620	46639	GAAGGCCAAATTTCATGTAT	34	448
1100701	2097	2116	46623	46642	ATTGAAGGCCAAATTTCATG	48	449
1100702	2105	2124	46631	46650	CTATTAAAATTGAAGGCCAA	77	450
1100703	2106	2125	46632	46651	GCTATTAAAATTGAAGGCCA	48	451
1100704	2108	2127	46634	46653	CTGCTATTAAAATTGAAGGC	25	452
1100705	2109	2128	46635	46654	ACTGCTATTAAAATTGAAGG	35	453
1100706	2110	2129	46636	46655	AACTGCTATTAAAATTGAAG	71	454
1100707	2111	2130	46637	46656	AAACTGCTATTAAAATTGAA	78	455
1100708	2112	2131	46638	46657	AAAACTGCTATTAAAATTGA	111	456
1100709	2168	2187	46694	46713	CATGACTCAACTGTAAAGAG	29	457
1100710	2204	2223	46730	46749	TACCTACTAAAAGATGTGAA	85	458
1100711	2205	2224	46731	46750	ATACCTACTAAAAGATGTGA	74	459
1100712	2206	2225	46732	46751	TATACCTACTAAAAGATGTG	77	460
1100713	2207	2226	46733	46752	CTATACCTACTAAAAGATGT	103	461
1100714	2208	2227	46734	46753	GCTATACCTACTAAAAGATG	55	462
1100715	2209	2228	46735	46754	AGCTATACCTACTAAAAGAT	63	463
1100716	2210	2229	46736	46755	AAGCTATACCTACTAAAAGA	73	464
1100718	2212	2231	46738	46757	ACAAGCTATACCTACTAAAA	60	465
1100720	2214	2233	46740	46759	TGACAAGCTATACCTACTAA	45	466
1100721	2216	2235	46742	46761	TTTGACAAGCTATACCTACT	57	467
1100722	2225	2244	46751	46770	ATCACCATCTTTGACAAGCT	30	468
1100723	2229	2248	46755	46774	CCAGATCACCATCTTTGACA	22	469
1100724	2231	2250	46757	46776	TTCCAGATCACCATCTTTGA	38	470
1100725	2232	2251	46758	46777	GTTCCAGATCACCATCTTTG	8	471
1100726	2233	2252	46759	46778	TGTTCCAGATCACCATCTTT	39	472
1100727	2234	2253	46760	46779	ATGTTCCAGATCACCATCTT	38	473
1100728	2236	2255	46762	46781	TCATGTTCCAGATCACCATC	83	474
1100729	2237	2256	46763	46782	TTCATGTTCCAGATCACCAT	16	475
1100730	2238	2257	46764	46783	TTTCATGTTCCAGATCACCA	15	476
1100731	2239	2258	46765	46784	TTTTCATGTTCCAGATCACC	22	477
1100732	2244	2263	46770	46789	AATTATTTTCATGTTCCAGA	12	478
1100733	2251	2270	46777	46796	ATTAGTAAATTATTTTCATG	76	479
1100734	2261	2280	46787	46806	ACATATTTTCATTAGTAAAT	131	480
1100735	2262	2281	46788	46807	AACATATTTTCATTAGTAAA	82	481

1100736	2273	2292	46799	46818	GTATAAATTTAAACATATTT	82	482
1100737	2276	2295	46802	46821	ACAGTATAAATTTAAACATA	101	483
1100738	2277	2296	46803	46822	CACAGTATAAATTTAAACAT	86	484
1100739	2278	2297	46804	46823	TCACAGTATAAATTTAAACA	96	485
1100740	2279	2298	46805	46824	ATCACAGTATAAATTTAAAC	116	486
1100741	2280	2299	46806	46825	AATCACAGTATAAATTTAAA	79	487
1100742	2282	2301	46808	46827	CAAATCACAGTATAAATTTA	92	488
1100743	2288	2307	46814	46833	AAGTGTCAAATCACAGTATA	58	489
1100744	2291	2310	46817	46836	TGCAAGTGTCAAATCACAGT	28	490
1100745	2305	2324	46831	46850	CTATCTAAACATGATGCAAG	63	491
1100746	2306	2325	46832	46851	GCTATCTAAACATGATGCAA	62	492
1100747	2307	2326	46833	46852	AGCTATCTAAACATGATGCA	87	493
1100748	2309	2328	46835	46854	TAAGCTATCTAAACATGATG	77	494
1100749	2310	2329	46836	46855	TTAAGCTATCTAAACATGAT	89	495
1100750	2311	2330	46837	46856	CTTAAGCTATCTAAACATGA	81	496
1100751	2312	2331	46838	46857	TCTTAAGCTATCTAAACATG	52	497
1100752	2314	2333	46840	46859	GTTCTTAAGCTATCTAAACA	63	498
1100754	2346	2365	46872	46891	TTATAGATCCACTAAGTACT	71	499
1100756	2355	2374	46881	46900	CTTTCTTATTTATAGATCCA	22	500
1100757	2357	2376	46883	46902	GACTTTCTTATTTATAGATC	32	501
1100758	2371	2390	46897	46916	TTATCAAAACTATGGACTTT	89	502
1100759	2372	2391	46898	46917	TTTATCAAAACTATGGACTT	61	503
1100760	2373	2392	46899	46918	ATTTATCAAAACTATGGACT	56	504
1100761	2375	2394	46901	46920	ATATTTATCAAAACTATGGA	87	505
1100762	2376	2395	46902	46921	AATATTTATCAAAACTATGG	75	506
1100763	2384	2403	46910	46929	TTAAAGAGAATATTTATCAA	123	507
1100764	2386	2405	46912	46931	AATTAAAGAGAATATTTATC	107	508
1100765	2392	2411	46918	46937	CATCTCAATTAAAGAGAATA	172	509
1100766	2395	2414	46921	46940	GTACATCTCAATTAAAGAGA	36	510
1100767	2422	2441	46948	46967	TCCTATTGACCCAGCAAGAA	38	511
1100768	2426	2445	46952	46971	ACTATCCTATTGACCCAGCA	24	512
1100769	2430	2449	46956	46975	TGATACTATCCTATTGACCC	25	513
1100770	2444	2463	46970	46989	GGTTTTCACCAAAATGATAC	50	514
1100771	2463	2482	46989	47008	ACATCAATTTCAGAGACATG	33	515
1100772	2464	2483	46990	47009	AACATCAATTTCAGAGACAT	24	516
1100773	2465	2484	46991	47010	AAACATCAATTTCAGAGACA	48	517
1100774	2472	2491	46998	47017	GAAACTAAAACATCAATTTC	104	518
1100775	2475	2494	47001	47020	ACTGAAACTAAAACATCAAT	114	519
1100776	2516	2535	47042	47061	AAAGAGCTTCAAAAGGAGAT	55	520
1100777	2525	2544	47051	47070	CAACATTCAAAAGAGCTTCA	40	521
1100778	2526	2545	47052	47071	TCAACATTCAAAAGAGCTTC	53	522
1100779	2527	2546	47053	47072	TTCAACATTCAAAAGAGCTT	65	523
1100780	2530	2549	47056	47075	CAATTCAACATTCAAAAGAG	64	524

1100781	2531	2550	47057	47076	ACAATTCAACATTCAAAAGA	97	525
1100782	2532	2551	47058	47077	AACAATTCAACATTCAAAAG	68	526
1100783	2533	2552	47059	47078	GAACAATTCAACATTCAAAA	39	527
1100784	2534	2553	47060	47079	TGAACAATTCAACATTCAAA	53	528
1100785	2535	2554	47061	47080	ATGAACAATTCAACATTCAA	57	529
1100786	2536	2555	47062	47081	TATGAACAATTCAACATTCA	67	530
1100787	2537	2556	47063	47082	TTATGAACAATTCAACATTC	50	531
1100788	2539	2558	47065	47084	GCTTATGAACAATTCAACAT	21	532
1100790	2543	2562	47069	47088	TTTAGCTTATGAACAATTCA	60	533
1100792	2553	2572	47079	47098	TTTCTTGGATTTTAGCTTAT	32	534
1100793	2561	2580	47087	47106	AGCTGAAATTTCTTGGATTT	48	535
1100794	2562	2581	47088	47107	CAGCTGAAATTTCTTGGATT	54	536
1100795	2563	2582	47089	47108	TCAGCTGAAATTTCTTGGAT	38	537
1100796	2564	2583	47090	47109	GTCAGCTGAAATTTCTTGGA	17	538
1100797	2566	2585	47092	47111	TTGTCAGCTGAAATTTCTTG	30	539
1100798	2568	2587	47094	47113	AGTTGTCAGCTGAAATTTCT	33	540
1100799	2569	2588	47095	47114	AAGTTGTCAGCTGAAATTTC	34	541
1100800	2570	2589	47096	47115	GAAGTTGTCAGCTGAAATTT	84	542
1100801	2571	2590	47097	47116	CGAAGTTGTCAGCTGAAATT	23	543
1100802	2572	2591	47098	47117	TCGAAGTTGTCAGCTGAAAT	16	544
1100803	2573	2592	47099	47118	TTCGAAGTTGTCAGCTGAAA	24	545
1100804	2574	2593	47100	47119	TTTCGAAGTTGTCAGCTGAA	26	546
1100805	2576	2595	47102	47121	ATTTTCGAAGTTGTCAGCTG	42	547
1100806	2583	2602	47109	47128	TATTATAATTTTCGAAGTTG	53	548
1100807	2585	2604	47111	47130	CATATTATAATTTTCGAAGT	71	549
1100808	2590	2609	47116	47135	TATACCATATTATAATTTTC	56	550
1100809	2595	2614	47121	47140	GGCAATATACCATATTATAA	14	551
1100810	2597	2616	47123	47142	AGGGCAATATACCATATTAT	17	552
1100811	2598	2617	47124	47143	GAGGGCAATATACCATATTA	25	553
1100812	2642	2661	47168	47187	ATCAAAAAACTTTCCCTGAT	79	554
1100813	2643	2662	47169	47188	GATCAAAAAACTTTCCCTGA	70	555
1100814	2644	2663	47170	47189	AGATCAAAAAACTTTCCCTG	58	556
1100815	2646	2665	47172	47191	CTAGATCAAAAAACTTTCCC	75	557
1100816	2647	2666	47173	47192	CCTAGATCAAAAAACTTTCC	58	558
1100817	2648	2667	47174	47193	TCCTAGATCAAAAAACTTTC	91	559
1100818	2649	2668	47175	47194	ATCCTAGATCAAAAAACTTT	62	560
1100819	2650	2669	47176	47195	AATCCTAGATCAAAAAACTT	62	561
1100820	2651	2670	47177	47196	AAATCCTAGATCAAAAAACT	92	562
1100821	2652	2671	47178	47197	TAAATCCTAGATCAAAAAAC	75	563
1100822	2656	2675	47182	47201	GCAATAAATCCTAGATCAAA	50	564
1100823	2657	2676	47183	47202	AGCAATAAATCCTAGATCAA	51	565
1100824	2658	2677	47184	47203	TAGCAATAAATCCTAGATCA	66	566
1100826	2660	2679	47186	47205	GTTAGCAATAAATCCTAGAT	29	567

1100828	2700	2719	47226	47245	AATCATAAATAAAAGATATT	87	568
1100829	2701	2720	47227	47246	TAATCATAAATAAAAGATAT	98	569
1100830	2712	2731	47238	47257	AAGCTATTTTATAATCATAA	72	570
1100831	2714	2733	47240	47259	AAAAGCTATTTTATAATCAT	78	571
1100832	2739	2758	47265	47284	CTTAAAAAATCTGTTATATC	78	572
1100833	2741	2760	47267	47286	GACTTAAAAAATCTGTTATA	83	573
1100834	2742	2761	47268	47287	TGACTTAAAAAATCTGTTAT	88	574
1100835	2743	2762	47269	47288	ATGACTTAAAAAATCTGTTA	67	575
1100836	2744	2763	47270	47289	AATGACTTAAAAAATCTGTT	77	576
1100837	2745	2764	47271	47290	TAATGACTTAAAAAATCTGT	83	577
1100838	2753	2772	47279	47298	GCACAAAATAATGACTTAAA	38	578
1100839	2754	2773	47280	47299	GGCACAAAATAATGACTTAA	8	579
1100840	2755	2774	47281	47300	TGGCACAAAATAATGACTTA	28	580
1100841	2756	2775	47282	47301	TTGGCACAAAATAATGACTT	42	581
1100842	2758	2777	47284	47303	GATTGGCACAAAATAATGAC	39	582
1100843	2778	2797	47304	47323	AAGGGAAACTTCAGAAAACT	41	583
1100844	2779	2798	47305	47324	TAAGGGAAACTTCAGAAAAC	74	584
1100845	2780	2799	47306	47325	GTAAGGGAAACTTCAGAAAA	42	585
1100846	2781	2800	47307	47326	TGTAAGGGAAACTTCAGAAA	24	586
1100847	2810	2829	47336	47355	TTAGATTTTAAAATAAAGCT	95	587
1100848	2830	2849	47356	47375	TTTAACTATTAAAAGAAACT	91	588
1100849	2840	2859	47366	47385	CTGAAACATTTTTAACTATT	60	589
1100850	2849	2868	47375	47394	ATAATTCTTCTGAAACATTT	59	590
1100851	2851	2870	47377	47396	TTATAATTCTTCTGAAACAT	58	591
1100852	2852	2871	47378	47397	TTTATAATTCTTCTGAAACA	79	592
1100853	2853	2872	47379	47398	TTTTATAATTCTTCTGAAAC	112	593
1100854	2854	2873	47380	47399	GTTTTATAATTCTTCTGAAA	58	594
1100855	2855	2874	47381	47400	AGTTTTATAATTCTTCTGAA	61	595
1100856	2856	2875	47382	47401	AAGTTTTATAATTCTTCTGA	59	596
1100857	2858	2877	47384	47403	TAAAGTTTTATAATTCTTCT	87	597
1100858	2859	2878	47385	47404	TTAAAGTTTTATAATTCTTC	79	598
1100859	2862	2881	47388	47407	GTTTTAAAGTTTTATAATTC	96	599
1100860	2867	2886	47393	47412	TTGCAGTTTTAAAGTTTTAT	82	600
1100862	2908	2927	47434	47453	TTTTTAAATCTTGAGGGAGT	51	601
1100864	2912	2931	47438	47457	TAGCTTTTTAAATCTTGAGG	11	602
1100865	2913	2932	47439	47458	TTAGCTTTTTAAATCTTGAG	11	603
1100866	2914	2933	47440	47459	TTTAGCTTTTTAAATCTTGA	60	604
1100867	2915	2934	47441	47460	ATTTAGCTTTTTAAATCTTG	84	605
1100868	2916	2935	47442	47461	TATTTAGCTTTTTAAATCTT	96	606
1100869	2924	2943	47450	47469	TCTTAAAATATTTAGCTTTT	87	607
1100870	2925	2944	47451	47470	GTCTTAAAATATTTAGCTTT	45	608
1100871	2926	2945	47452	47471	AGTCTTAAAATATTTAGCTT	58	609
1100872	2927	2946	47453	47472	CAGTCTTAAAATATTTAGCT	85	610

1100873	2928	2947	47454	47473	TCAGTCTTAAAATATTTAGC	7	611
1100874	2929	2948	47455	47474	TTCAGTCTTAAAATATTTAG	78	612
1100875	2930	2949	47456	47475	GTTCAGTCTTAAAATATTTA	26	613
1100876	2932	2951	47458	47477	ATGTTCAGTCTTAAAATATT	47	614
1100877	2935	2954	47461	47480	TAAATGTTCAGTCTTAAAAT	98	615
1100878	2936	2955	47462	47481	ATAAATGTTCAGTCTTAAAA	94	616
1100879	2948	2967	47474	47493	GTAATAATTAACATAAATGT	95	617
1100880	2951	2970	47477	47496	CTGGTAATAATTAACATAAA	110	618
1100881	2952	2971	47478	47497	ACTGGTAATAATTAACATAA	54	619
1100882	2974	2993	47500	47519	CCATGGAAAATATGACAAAC	44	620
1100883	2982	3001	47508	47527	ACAAATATCCATGGAAAATA	76	621
1100884	2983	3002	47509	47528	AACAAATATCCATGGAAAAT	70	622
1100885	2984	3003	47510	47529	GAACAAATATCCATGGAAAA	43	623
1100886	2985	3004	47511	47530	TGAACAAATATCCATGGAAA	49	624
1100887	2987	3006	47513	47532	AATGAACAAATATCCATGGA	50	625
1100888	2988	3007	47514	47533	TAATGAACAAATATCCATGG	43	626
1100889	2989	3008	47515	47534	GTAATGAACAAATATCCATG	27	627
1100890	2990	3009	47516	47535	GGTAATGAACAAATATCCAT	52	628
1100891	2991	3010	47517	47536	AGGTAATGAACAAATATCCA	40	629
1100892	2996	3015	47522	47541	GAAAAAGGTAATGAACAAAT	84	630
1100893	3031	3050	47557	47576	CAAGTGTATGAAAAGTTTAA	75	631
1100894	3038	3057	47564	47583	ATCAATTCAAGTGTATGAAA	83	632
1100895	3040	3059	47566	47585	TCATCAATTCAAGTGTATGA	35	633
1100896	3041	3060	47567	47586	CTCATCAATTCAAGTGTATG	42	634
1100898	3043	3062	47569	47588	AGCTCATCAATTCAAGTGTA	18	635
1100900	3045	3064	47571	47590	GTAGCTCATCAATTCAAGTG	16	636
1100901	3046	3065	47572	47591	GGTAGCTCATCAATTCAAGT	17	637
1100902	3047	3066	47573	47592	AGGTAGCTCATCAATTCAAG	20	638
1100903	3048	3067	47574	47593	TAGGTAGCTCATCAATTCAA	16	639
1100904	3049	3068	47575	47594	TTAGGTAGCTCATCAATTCA	33	640
1100905	3051	3070	47577	47596	TATTAGGTAGCTCATCAATT	36	641
1100906	3060	3079	47586	47605	TCATTTTTATATTAGGTAGC	15	642
1100907	3061	3080	47587	47606	CTCATTTTTATATTAGGTAG	11	643
1100908	3062	3081	47588	47607	TCTCATTTTTATATTAGGTA	112	644
1100909	3069	3088	47595	47614	TTGGTTTTCTCATTTTTATA	23	645
1100910	3070	3089	47596	47615	ATTGGTTTTCTCATTTTTAT	21	646
1100911	3071	3090	47597	47616	TATTGGTTTTCTCATTTTTA	15	647
1100912	3072	3091	47598	47617	ATATTGGTTTTCTCATTTTT	34	648
1100913	3073	3092	47599	47618	CATATTGGTTTTCTCATTTT	24	649
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	8	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45

1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	78	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
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1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	4	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	9	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
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1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
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1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	6	45
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1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	7	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	5	45
1100915	3075	3094	47601	47620	TGCATATTGGTTTTCTCATT	8	650
1100916	3076	3095	47602	47621	ATGCATATTGGTTTTCTCAT	10	651
1100917	3077	3096	47603	47622	AATGCATATTGGTTTTCTCA	8	652
1100918	3079	3098	47605	47624	AAAATGCATATTGGTTTTCT	22	653
1100919	3116	3135	47642	47661	TATATATGAACTTTATAAAC	74	654
1100920	3119	3138	47645	47664	GGGTATATATGAACTTTATA	8	655
1100921	3122	3141	47648	47667	CTAGGGTATATATGAACTTT	21	656
1100922	3123	3142	47649	47668	ACTAGGGTATATATGAACTT	24	657
1100923	3124	3143	47650	47669	AACTAGGGTATATATGAACT	24	658
1100924	3133	3152	47659	47678	AAGTGCTTTAACTAGGGTAT	16	659
1100925	3134	3153	47660	47679	TAAGTGCTTTAACTAGGGTA	19	660
1100926	3135	3154	47661	47680	TTAAGTGCTTTAACTAGGGT	55	661
1100927	3140	3159	47666	47685	TTTTCTTAAGTGCTTTAACT	53	662

1100928	3146	3165	47672	47691	GCCATATTTTCTTAAGTGCT	18	663
1100929	3162	3181	47688	47707	ACTAAAAGTCAAACATGCCA	43	664
1100930	3164	3183	47690	47709	GAACTAAAAGTCAAACATGC	44	665
1100931	3507	3526	48033	48052	GCTCTGCTTTAAAAACTCTC	89	666
1100932	3536	3555	48062	48081	CACATTCAAACGCATCCAGT	49	667
1100933	3537	3556	48063	48082	ACACATTCAAACGCATCCAG	39	668
1100935	3540	3559	48066	48085	CAAACACATTCAAACGCATC	85	669
1100937	3542	3561	48068	48087	CACAAACACATTCAAACGCA	69	670
1100938	3544	3563	48070	48089	TACACAAACACATTCAAACG	76	671
1100939	3545	3564	48071	48090	CTACACAAACACATTCAAAC	57	672
1100940	3546	3565	48072	48091	ACTACACAAACACATTCAAA	82	673
1100941	3549	3568	48075	48094	CAAACTACACAAACACATTC	76	674
1100942	3550	3569	48076	48095	ACAAACTACACAAACACATT	95	675
1100943	3551	3570	48077	48096	AACAAACTACACAAACACAT	66	676
1100944	3554	3573	48080	48099	CACAACAAACTACACAAACA	65	677
1100945	3555	3574	48081	48100	TCACAACAAACTACACAAAC	92	678
1100946	3556	3575	48082	48101	TTCACAACAAACTACACAAA	88	679
1100947	3558	3577	48084	48103	ATTTCACAACAAACTACACA	78	680
1100948	3559	3578	48085	48104	AATTTCACAACAAACTACAC	66	681
1100949	3560	3579	48086	48105	CAATTTCACAACAAACTACA	93	682
1100950	3563	3582	48089	48108	TAACAATTTCACAACAAACT	89	683
1100951	3564	3583	48090	48109	GTAACAATTTCACAACAAAC	38	684
1100952	3565	3584	48091	48110	TGTAACAATTTCACAACAAA	52	685
1100953	3566	3585	48092	48111	ATGTAACAATTTCACAACAA	35	686
1100954	3567	3586	48093	48112	AATGTAACAATTTCACAACA	61	687
1100955	3568	3587	48094	48113	AAATGTAACAATTTCACAAC	73	688
1100956	3569	3588	48095	48114	TAAATGTAACAATTTCACAA	104	689
1100957	3570	3589	48096	48115	CTAAATGTAACAATTTCACA	87	690
1100958	3571	3590	48097	48116	GCTAAATGTAACAATTTCAC	46	691
1100959	3576	3595	48102	48121	TGCCTGCTAAATGTAACAAT	66	692
1100960	3582	3601	48108	48127	TGGATCTGCCTGCTAAATGT	42	693
1100961	3616	3635	48142	48161	CAACCCCACCAAGATGACAG	68	694
1100962	3621	3640	48147	48166	TAAGCCAACCCCACCAAGAT	88	695
1100963	3622	3641	48148	48167	TTAAGCCAACCCCACCAAGA	53	696
1100964	3626	3645	48152	48171	AAATTTAAGCCAACCCCACC	83	697
1100965	3627	3646	48153	48172	TAAATTTAAGCCAACCCCAC	134	698
1100966	3633	3652	48159	48178	GTCAATTAAATTTAAGCCAA	41	699
1100967	3636	3655	48162	48181	ACAGTCAATTAAATTTAAGC	72	700
1100968	3644	3663	48170	48189	GAATCTAAACAGTCAATTAA	75	701
1100969	3648	3667	48174	48193	AATGGAATCTAAACAGTCAA	78	702
1100971	3668	3687	48194	48213	TACTGGCCAATCAATTAAGA	73	703
1100973	3672	3691	48198	48217	TTCATACTGGCCAATCAATT	60	704
1100974	3674	3693	48200	48219	TTTTCATACTGGCCAATCAA	64	705

1100975	3676	3695	48202	48221	TCTTTTCATACTGGCCAATC	71	706
1100976	3677	3696	48203	48222	ATCTTTTCATACTGGCCAAT	52	707
1100977	3678	3697	48204	48223	CATCTTTTCATACTGGCCAA	50	708
1100978	3679	3698	48205	48224	GCATCTTTTCATACTGGCCA	35	709
1100979	3680	3699	48206	48225	GGCATCTTTTCATACTGGCC	29	710
1100980	3681	3700	48207	48226	TGGCATCTTTTCATACTGGC	14	711
1100981	3682	3701	48208	48227	CTGGCATCTTTTCATACTGG	104	712
1100982	3684	3703	48210	48229	CACTGGCATCTTTTCATACT	28	713
1100983	3699	3718	48225	48244	TACTATGGTTACTTGCACTG	35	714
1100984	3730	3749	48256	48275	TATAGCTTTGAATAATTTTT	121	715
1100985	3740	3759	48266	48285	ATGTATAAACTATAGCTTTG	37	716
1100986	3742	3761	48268	48287	TGATGTATAAACTATAGCTT	53	717
1100987	3747	3766	48273	48292	GTACCTGATGTATAAACTAT	51	718
1100988	3749	3768	48275	48294	CAGTACCTGATGTATAAACT	21	719
1100989	3750	3769	48276	48295	GCAGTACCTGATGTATAAAC	11	720
1100990	3751	3770	48277	48296	GGCAGTACCTGATGTATAAA	10	721
1100991	3752	3771	48278	48297	TGGCAGTACCTGATGTATAA	10	722
1100992	3753	3772	48279	48298	ATGGCAGTACCTGATGTATA	16	723
1100993	3754	3773	48280	48299	AATGGCAGTACCTGATGTAT	48	724
1100994	3755	3774	48281	48300	AAATGGCAGTACCTGATGTA	40	725
1100995	3757	3776	48283	48302	GTAAATGGCAGTACCTGATG	15	726
1100996	3764	3783	48290	48309	GTTTACAGTAAATGGCAGTA	18	727
1100997	3766	3785	48292	48311	TGGTTTACAGTAAATGGCAG	16	728
1100998	3768	3787	48294	48313	GGTGGTTTACAGTAAATGGC	25	729
1100999	3769	3788	48295	48314	AGGTGGTTTACAGTAAATGG	17	730
1101000	3771	3790	48297	48316	GCAGGTGGTTTACAGTAAAT	13	731
1101001	3782	3801	48308	48327	CTGACTTTCTTGCAGGTGGT	21	732
1101002	3785	3804	48311	48330	TTCCTGACTTTCTTGCAGGT	102	733
1101003	3786	3805	48312	48331	GTTCCTGACTTTCTTGCAGG	45	734
1101004	3788	3807	48314	48333	TTGTTCCTGACTTTCTTGCA	27	735
1101005	3791	3810	48317	48336	TAGTTGTTCCTGACTTTCTT	50	736
1101007	3793	3812	48319	48338	TTTAGTTGTTCCTGACTTTC	74	737
1101009	3838	3857	48364	48383	AATGGAAATCTTTAATACAC	64	738
1101010	3854	3873	48380	48399	CCAATTAGTAAAACAAAATG	104	739
1101011	3861	3880	48387	48406	GATGTTCCCAATTAGTAAAA	29	740
1101012	3863	3882	48389	48408	AAGATGTTCCCAATTAGTAA	29	741
1101013	3864	3883	48390	48409	TAAGATGTTCCCAATTAGTA	47	742
1101014	3870	3889	48396	48415	AAACATTAAGATGTTCCCAA	35	743
1101015	3871	3890	48397	48416	TAAACATTAAGATGTTCCCA	45	744
1101016	3873	3892	48399	48418	ATTAAACATTAAGATGTTCC	55	745
1101017	3874	3893	48400	48419	TATTAAACATTAAGATGTTC	90	746
1101018	3875	3894	48401	48420	ATATTAAACATTAAGATGTT	113	747
1101019	3877	3896	48403	48422	AAATATTAAACATTAAGATG	86	748

1101020	3878	3897	48404	48423	TAAATATTAAACATTAAGAT	90	749
1101021	3884	3903	48410	48429	ATAGTTTAAATATTAAACAT	99	750
1101022	3886	3905	48412	48431	CAATAGTTTAAATATTAAAC	119	751
1101023	3887	3906	48413	48432	CCAATAGTTTAAATATTAAA	111	752
1101024	3888	3907	48414	48433	ACCAATAGTTTAAATATTAA	98	753
1101025	3890	3909	48416	48435	ATACCAATAGTTTAAATATT	110	754
1101026	3896	3915	48422	48441	AAAATGATACCAATAGTTTA	78	755
1101027	3897	3916	48423	48442	AAAAATGATACCAATAGTTT	96	756
1101028	3898	3917	48424	48443	GAAAAATGATACCAATAGTT	67	757
1101029	3899	3918	48425	48444	AGAAAAATGATACCAATAGT	61	758
1101030	3900	3919	48426	48445	TAGAAAAATGATACCAATAG	61	759
1101031	3902	3921	48428	48447	ATTAGAAAAATGATACCAAT	75	760
1101032	3903	3922	48429	48448	CATTAGAAAAATGATACCAA	74	761
1101033	3905	3924	48431	48450	TACATTAGAAAAATGATACC	74	762
1101034	3906	3925	48432	48451	ATACATTAGAAAAATGATAC	119	763
1101035	3907	3926	48433	48452	TATACATTAGAAAAATGATA	94	764
1101036	3912	3931	48438	48457	CAAATTATACATTAGAAAAA	138	765
1101037	3913	3932	48439	48458	ACAAATTATACATTAGAAAA	83	766
1101038	3914	3933	48440	48459	TACAAATTATACATTAGAAA	70	767
1101039	3915	3934	48441	48460	ATACAAATTATACATTAGAA	113	768
1101040	3916	3935	48442	48461	AATACAAATTATACATTAGA	105	769
1101041	3917	3936	48443	48462	TAATACAAATTATACATTAG	85	770
1101043	3919	3938	48445	48464	AGTAATACAAATTATACATT	98	771
1101045	3922	3941	48448	48467	CCCAGTAATACAAATTATAC	74	772
1101046	3923	3942	48449	48468	TCCCAGTAATACAAATTATA	50	773
1101047	3924	3943	48450	48469	ATCCCAGTAATACAAATTAT	40	774
1101048	3925	3944	48451	48470	GATCCCAGTAATACAAATTA	47	775
1101049	3929	3948	48455	48474	ACTTGATCCCAGTAATACAA	21	776
1101050	3930	3949	48456	48475	TACTTGATCCCAGTAATACA	30	777
1101051	3931	3950	48457	48476	ATACTTGATCCCAGTAATAC	32	778
1101052	3932	3951	48458	48477	CATACTTGATCCCAGTAATA	29	779
1101053	3935	3954	48461	48480	GTACATACTTGATCCCAGTA	89	780
1101054	3937	3956	48463	48482	CTGTACATACTTGATCCCAG	15	781
1101055	3941	3960	48467	48486	ACCACTGTACATACTTGATC	32	782
1101056	3942	3961	48468	48487	CACCACTGTACATACTTGAT	45	783
1101057	3947	3966	48473	48492	AGCATCACCACTGTACATAC	15	784
1101058	3948	3967	48474	48493	TAGCATCACCACTGTACATA	23	785
1101059	3950	3969	48476	48495	ACTAGCATCACCACTGTACA	79	786
1101060	3951	3970	48477	48496	TACTAGCATCACCACTGTAC	74	787
1101061	3960	3979	48486	48505	TTAAACTTCTACTAGCATCA	56	788
1101062	3964	3983	48490	48509	AGGCTTAAACTTCTACTAGC	33	789
1101063	3968	3987	48494	48513	TCCAAGGCTTAAACTTCTAC	27	790
1101064	3977	3996	48503	48522	AGTGGTATTTCCAAGGCTTA	23	791

1101065	3978	3997	48504	48523	AAGTGGTATTTCCAAGGCTT	13	792
1101066	3979	3998	48505	48524	AAAGTGGTATTTCCAAGGCT	18	793
1101067	3989	4008	48515	48534	TGAAAATATGAAAGTGGTAT	30	794
1101068	3990	4009	48516	48535	CTGAAAATATGAAAGTGGTA	47	795
1101069	3993	4012	48519	48538	CATCTGAAAATATGAAAGTG	105	796
1101070	3994	4013	48520	48539	ACATCTGAAAATATGAAAGT	111	797
1101071	3995	4014	48521	48540	GACATCTGAAAATATGAAAG	25	798
1101072	3996	4015	48522	48541	TGACATCTGAAAATATGAAA	84	799
1101073	3997	4016	48523	48542	ATGACATCTGAAAATATGAA	48	800
1101074	4004	4023	48530	48549	TAAATCCATGACATCTGAAA	59	801
1101075	4007	4026	48533	48552	CATTAAATCCATGACATCTG	36	802
1101076	4008	4027	48534	48553	TCATTAAATCCATGACATCT	51	803
1101077	4009	4028	48535	48554	CTCATTAAATCCATGACATC	96	804
1101079	4011	4030	48537	48556	TACTCATTAAATCCATGACA	53	805
1101081	4013	4032	48539	48558	ATTACTCATTAAATCCATGA	60	806
1101082	4015	4034	48541	48560	AAATTACTCATTAAATCCAT	62	807
1101083	4016	4035	48542	48561	TAAATTACTCATTAAATCCA	102	808
1101084	4017	4036	48543	48562	ATAAATTACTCATTAAATCC	71	809
1101085	4018	4037	48544	48563	CATAAATTACTCATTAAATC	75	810
1101086	4019	4038	48545	48564	ACATAAATTACTCATTAAAT	126	811
1101087	4020	4039	48546	48565	AACATAAATTACTCATTAAA	81	812
1101088	4021	4040	48547	48566	AAACATAAATTACTCATTAA	78	813
1101089	4022	4041	48548	48567	AAAACATAAATTACTCATTA	103	814
1101090	4023	4042	48549	48568	AAAAACATAAATTACTCATT	98	815
1101091	4044	4063	48570	48589	AGATTAACTATTCTGAATTT	89	816
1101092	4045	4064	48571	48590	GAGATTAACTATTCTGAATT	46	817
1101093	4046	4065	48572	48591	AGAGATTAACTATTCTGAAT	47	818
1101094	4047	4066	48573	48592	CAGAGATTAACTATTCTGAA	57	819
1101095	4048	4067	48574	48593	TCAGAGATTAACTATTCTGA	74	820
1101096	4051	4070	48577	48596	AGATCAGAGATTAACTATTC	34	821
1101097	4052	4071	48578	48597	TAGATCAGAGATTAACTATT	42	822
1101098	4057	4076	48583	48602	GGTTTTAGATCAGAGATTAA	22	823
1101099	4058	4077	48584	48603	TGGTTTTAGATCAGAGATTA	17	824
1101100	4059	4078	48585	48604	ATGGTTTTAGATCAGAGATT	23	825
1101101	4061	4080	48587	48606	TGATGGTTTTAGATCAGAGA	8	826
1101102	4079	4098	48605	48624	ACCGTAAAAAACATAGATTG	47	827
1101103	4081	4100	48607	48626	TTACCGTAAAAAACATAGAT	62	828
1101104	4099	4118	48625	48644	ACTGAAATATTTACATGATT	67	829
1101105	4108	4127	48634	48653	GTTTATATTACTGAAATATT	86	830
1101106	4111	4130	48637	48656	ACAGTTTATATTACTGAAAT	116	831
1101107	4112	4131	48638	48657	AACAGTTTATATTACTGAAA	91	832
1101108	4113	4132	48639	48658	AAACAGTTTATATTACTGAA	86	833
1101109	4114	4133	48640	48659	CAAACAGTTTATATTACTGA	116	834

1101110	4115	4134	48641	48660	TCAAACAGTTTATATTACTG	70	835
1101111	4117	4136	48643	48662	TTTCAAACAGTTTATATTAC	86	836
1101112	4120	4139	48646	48665	CCTTTTCAAACAGTTTATAT	63	837
1101113	4121	4140	48647	48666	GCCTTTTCAAACAGTTTATA	36	838
1101115	4124	4143	48650	48669	GCAGCCTTTTCAAACAGTTT	31	839
1101117	4126	4145	48652	48671	CAGCAGCCTTTTCAAACAGT	27	840
1101118	4128	4147	48654	48673	TGCAGCAGCCTTTTCAAACA	36	841
1101119	4138	4157	48664	48683	AGAGTTTACCTGCAGCAGCC	36	842
1101120	4140	4159	48666	48685	ATAGAGTTTACCTGCAGCAG	21	843
1101121	4141	4160	48667	48686	TATAGAGTTTACCTGCAGCA	14	844
1101122	4142	4161	48668	48687	GTATAGAGTTTACCTGCAGC	15	845
1101123	4144	4163	48670	48689	TAGTATAGAGTTTACCTGCA	32	846
1101124	4169	4188	48695	48714	ATTGTAAATTATTTGGCCAA	78	847
1101125	4170	4189	48696	48715	AATTGTAAATTATTTGGCCA	84	848
1101126	4171	4190	48697	48716	GAATTGTAAATTATTTGGCC	57	849
1101127	4172	4191	48698	48717	TGAATTGTAAATTATTTGGC	44	850
1101128	4173	4192	48699	48718	GTGAATTGTAAATTATTTGG	26	851
1101129	4178	4197	48704	48723	ATTCTGTGAATTGTAAATTA	42	852
1101130	4191	4210	48717	48736	CCTTAAATAAAATATTCTGT	87	853
1101131	4197	4216	48723	48742	GCACCACCTTAAATAAAATA	62	854
1101132	4200	4219	48726	48745	AAAGCACCACCTTAAATAAA	83	855
1101133	4224	4243	48750	48769	ATCAAGTTTTAAGGACAAAA	56	856
1101134	4226	4245	48752	48771	AAATCAAGTTTTAAGGACAA	88	857
1101135	4227	4246	48753	48772	AAAATCAAGTTTTAAGGACA	84	858
1101136	4228	4247	48754	48773	AAAAATCAAGTTTTAAGGAC	94	859
1101137	4236	4255	48762	48781	AAGTTAAGAAAAATCAAGTT	82	860
1101138	4253	4272	48779	48798	CTTTGGCATCATGAATAAAG	35	861
1101139	4330	4349	48856	48875	AATATTAAACAATATGGACT	54	862
1101140	4332	4351	48858	48877	TTAATATTAAACAATATGGA	88	863
1101141	4334	4353	48860	48879	ACTTAATATTAAACAATATG	114	864
1101142	4335	4354	48861	48880	AACTTAATATTAAACAATAT	87	865
1101143	4343	4362	48869	48888	TTTTATTCAACTTAATATTA	100	866
1101144	4352	4371	48878	48897	TAAAATTTATTTTATTCAAC	99	867
1101145	4380	4399	48906	48925	CAAAATGTGATTTAGGCTCT	34	868
1101146	4389	4408	48915	48934	TCAGACAATCAAAATGTGAT	44	869
1101147	4397	4416	48923	48942	TCAAAAATTCAGACAATCAA	85	870
1101148	4399	4418	48925	48944	TATCAAAAATTCAGACAATC	74	871
1101149	4400	4419	48926	48945	GTATCAAAAATTCAGACAAT	71	872
1101151	4403	4422	48929	48948	ATAGTATCAAAAATTCAGAC	84	873
1101153	4758	4777	49284	49303	GGTTTTAAGAATTTAGTAGC	26	874
1101154	4759	4778	49285	49304	CGGTTTTAAGAATTTAGTAG	57	875
1101155	4762	4781	49288	49307	GGCCGGTTTTAAGAATTTAG	74	876
1101156	4793	4812	49319	49338	GAATCTATTTTTTATCTGTA	33	877

1101157	4820	4839	49346	49365	AAAATTATCATATTTTGATT	76	878
1101158	4821	4840	49347	49366	TAAAATTATCATATTTTGAT	97	879
1101159	4827	4846	49353	49372	AGATTTTAAAATTATCATAT	79	880
1101160	4831	4850	49357	49376	CTTAAGATTTTAAAATTATC	94	881
1101161	4834	4853	49360	49379	CTACTTAAGATTTTAAAATT	116	882
1101162	4841	4860	49367	49386	TATTTTTCTACTTAAGATTT	81	883
1101163	4843	4862	49369	49388	TTTATTTTTCTACTTAAGAT	130	884
1101164	4845	4864	49371	49390	GATTTATTTTTCTACTTAAG	85	885
1101165	4850	4869	49376	49395	ATCAAGATTTATTTTTCTAC	54	886
1101166	4851	4870	49377	49396	CATCAAGATTTATTTTTCTA	79	887
1101167	4853	4872	49379	49398	AACATCAAGATTTATTTTTC	90	888
1101168	4859	4878	49385	49404	ATTTAAAACATCAAGATTTA	98	889
1101169	4864	4883	49390	49409	TAAGAATTTAAAACATCAAG	63	890
1101170	4865	4884	49391	49410	GTAAGAATTTAAAACATCAA	76	891
1101171	4887	4906	49413	49432	CAATATTAACTATTGAATCC	88	892
1101172	5256	5275	49782	49801	ATAAAGTTTTTAATAGGAAG	99	893
1101173	5258	5277	49784	49803	GGATAAAGTTTTTAATAGGA	52	894
1101174	5556	5575	50082	50101	CAAACAAACCTTTAAGATGG	95	895
1101175	5557	5576	50083	50102	ACAAACAAACCTTTAAGATG	93	896
1101176	5575	5594	50101	50120	TTTCCGGATTAAAAAAAAAC	103	897
1101177	5801	5820	50327	50346	AAAAAAAACAAATATTCGCC	88	898
1101178	5802	5821	50328	50347	TAAAAAAAACAAATATTCGC	101	899
1101179	5947	5966	50473	50492	AAACAATTCACTTTGAAAAC	74	900
1101180	5950	5969	50476	50495	AACAAACAATTCACTTTGAA	62	901
1101181	5951	5970	50477	50496	CAACAAACAATTCACTTTGA	67	902
1101182	5952	5971	50478	50497	ACAACAAACAATTCACTTTG	44	903
1101183	5953	5972	50479	50498	TACAACAAACAATTCACTTT	102	904
1101184	5954	5973	50480	50499	ATACAACAAACAATTCACTT	63	905
1101185	5955	5974	50481	50500	GATACAACAAACAATTCACT	56	906
1101187	5958	5977	50484	50503	CTCGATACAACAAACAATTC	63	907
1101189	5960	5979	50486	50505	GACTCGATACAACAAACAAT	54	908
1101190	5961	5980	50487	50506	GGACTCGATACAACAAACAA	63	909
1101191	5962	5981	50488	50507	AGGACTCGATACAACAAACA	41	910
1101192	5963	5982	50489	50508	AAGGACTCGATACAACAAAC	38	911
1101193	5965	5984	50491	50510	TTAAGGACTCGATACAACAA	55	912
1101194	5976	5995	50502	50521	TATATCCATACTTAAGGACT	70	913
1101195	5986	6005	50512	50531	GGGTCACATATATATCCATA	71	914
1101196	5988	6007	50514	50533	TAGGGTCACATATATATCCA	51	915
1101197	5992	6011	50518	50537	TAATTAGGGTCACATATATA	98	916
1101198	5994	6013	50520	50539	CTTAATTAGGGTCACATATA	46	917
1101199	5995	6014	50521	50540	TCTTAATTAGGGTCACATAT	35	918
1101200	5996	6015	50522	50541	TTCTTAATTAGGGTCACATA	45	919
1101201	5997	6016	50523	50542	GTTCTTAATTAGGGTCACAT	20	920

1101202	5998	6017	50524	50543	AGTTCTTAATTAGGGTCACA	18	921
1101203	5999	6018	50525	50544	TAGTTCTTAATTAGGGTCAC	20	922
1101204	6000	6019	50526	50545	GTAGTTCTTAATTAGGGTCA	21	923
1101205	6002	6021	50528	50547	TGGTAGTTCTTAATTAGGGT	25	924
1101206	6018	6037	50544	50563	ATTAGTTGATCCAATCTGGT	52	925
1101207	6019	6038	50545	50564	GATTAGTTGATCCAATCTGG	40	926
1101208	6028	6047	50554	50573	TGCTGACATGATTAGTTGAT	41	927
1101209	6029	6048	50555	50574	TTGCTGACATGATTAGTTGA	51	928
1101210	6032	6051	50558	50577	ACATTGCTGACATGATTAGT	54	929
1101211	6041	6060	50567	50586	AAGTTATTTACATTGCTGAC	34	930
1101212	6044	6063	50570	50589	ATAAAGTTATTTACATTGCT	72	931
1101213	6045	6064	50571	50590	AATAAAGTTATTTACATTGC	86	932
1101214	6056	6075	50582	50601	TGAATATGAAAAATAAAGTT	112	933
1101215	6067	6086	50593	50612	AGTTTTTATTTTGAATATGA	75	934
1101216	6071	6090	50597	50616	AGAAAGTTTTTATTTTGAAT	99	935
1101217	6121	6140	50647	50666	GTCATTTTTTAAAGCAAAAA	110	936
1101218	6124	6143	50650	50669	CAGGTCATTTTTTAAAGCAA	32	937
1101219	6135	6154	50661	50680	AAATACAAAGCCAGGTCATT	64	938
1101220	6141	6160	50667	50686	CTAAAAAAATACAAAGCCAG	111	939
1101221	6142	6161	50668	50687	ACTAAAAAAAATACAAAGCCA	55	940
1101223	6151	6170	50677	50696	ATGTTTAAGACTAAAAAAAT	90	941
1101225	6201	6220	50727	50746	GTCAATAATCTTCACTCATG	47	942
1101226	6205	6224	50731	50750	CGATGTCAATAATCTTCACT	71	943
1101227	6214	6233	50740	50759	ATTTACCAACGATGTCAATA	58	944
1101228	6216	6235	50742	50761	GAATTTACCAACGATGTCAA	58	945
1101229	6219	6238	50745	50764	CTAGAATTTACCAACGATGT	49	946
1101230	6223	6242	50749	50768	AATTCTAGAATTTACCAACG	57	947
1101231	6224	6243	50750	50769	AAATTCTAGAATTTACCAAC	63	948
1101232	6225	6244	50751	50770	AAAATTCTAGAATTTACCAA	101	949
1101233	6228	6247	50754	50773	ATCAAAATTCTAGAATTTAC	85	950
1101234	6230	6249	50756	50775	AAATCAAAATTCTAGAATTT	95	951
1101235	6232	6251	50758	50777	CAAAATCAAAATTCTAGAAT	107	952
1101236	6301	6320	50827	50846	ACTAATTCTTAAAATGCCAG	66	953
1101237	6302	6321	50828	50847	CACTAATTCTTAAAATGCCA	64	954
1101238	6332	6351	50858	50877	TTACGACAAATTTAGAAGTT	100	955
1101239	6341	6360	50867	50886	ACATGCCAATTACGACAAAT	65	956
1101240	6351	6370	50877	50896	ATGCTATTAAACATGCCAAT	52	957
1101241	6353	6372	50879	50898	ATATGCTATTAAACATGCCA	28	958
1101242	6354	6373	50880	50899	GATATGCTATTAAACATGCC	75	959
1101243	6355	6374	50881	50900	TGATATGCTATTAAACATGC	63	960
1101244	6363	6382	50889	50908	ATGTTTTTTGATATGCTATT	60	961
1101245	6364	6383	50890	50909	AATGTTTTTTGATATGCTAT	38	962
1101246	6365	6384	50891	50910	AAATGTTTTTTGATATGCTA	69	963

1101247	6366	6385	50892	50911	AAAATGTTTTTTGATATGCT	75	964
1101248	6376	6395	50902	50921	CCACAGGCTTAAAATGTTTT	87	965
1101249	6384	6403	50910	50929	CTATGAATCCACAGGCTTAA	47	966
1101250	6406	6425	50932	50951	CTAATGTTTCTCATTGCTTT	48	967
1101251	6420	6439	50946	50965	CCATTTATATTTTACTAATG	91	968
1101252	6423	6442	50949	50968	TATCCATTTATATTTTACTA	59	969
1101253	6427	6446	50953	50972	GGAATATCCATTTATATTTT	53	970
1101254	6447	6466	50973	50992	AGAGCTTCCTAAATGCATCA	62	971
1101255	6480	6499	51006	51025	AAAACATTCCTTGAACTATG	71	972
1101256	6482	6501	51008	51027	AGAAAACATTCCTTGAACTA	71	973
1101257	6484	6503	51010	51029	TCAGAAAACATTCCTTGAAC	77	974
1101259	6546	6565	51072	51091	GATAATCACATTTAAAAATG	82	975
1101261	6552	6571	51078	51097	AAATTAGATAATCACATTTA	107	976
1101262	6553	6572	51079	51098	AAAATTAGATAATCACATTT	95	977
1101263	6554	6573	51080	51099	AAAAATTAGATAATCACATT	112	978
1101264	6555	6574	51081	51100	TAAAAATTAGATAATCACAT	81	979
1101265	6557	6576	51083	51102	TGTAAAAATTAGATAATCAC	103	980
1101266	6560	6579	51086	51105	TGTTGTAAAAATTAGATAAT	119	981
1101267	6561	6580	51087	51106	GTGTTGTAAAAATTAGATAA	73	982
1101268	6562	6581	51088	51107	AGTGTTGTAAAAATTAGATA	88	983
1101269	6563	6582	51089	51108	CAGTGTTGTAAAAATTAGAT	81	984
1101270	6571	6590	51097	51116	TAATAGCCCAGTGTTGTAAA	46	985
1101271	6573	6592	51099	51118	CCTAATAGCCCAGTGTTGTA	39	986
1101272	6574	6593	51100	51119	TCCTAATAGCCCAGTGTTGT	48	987
1101273	6575	6594	51101	51120	TTCCTAATAGCCCAGTGTTG	49	988
1101274	6580	6599	51106	51125	AGTTATTCCTAATAGCCCAG	38	989
1101275	6581	6600	51107	51126	AAGTTATTCCTAATAGCCCA	56	990
1101276	6582	6601	51108	51127	AAAGTTATTCCTAATAGCCC	52	991
1101277	6583	6602	51109	51128	AAAAGTTATTCCTAATAGCC	60	992
1101278	6584	6603	51110	51129	AAAAAGTTATTCCTAATAGC	81	993
1101279	6585	6604	51111	51130	TAAAAAGTTATTCCTAATAG	78	994
1101280	6587	6606	51113	51132	TTTAAAAAGTTATTCCTAAT	108	995
1101281	6600	6619	51126	51145	CAGAACAGTAATTTTTAAAA	106	996
1101282	6604	6623	51130	51149	TATACAGAACAGTAATTTTT	64	997
1101283	6605	6624	51131	51150	TTATACAGAACAGTAATTTT	85	998
1101284	6606	6625	51132	51151	TTTATACAGAACAGTAATTT	95	999
1101285	6607	6626	51133	51152	ATTTATACAGAACAGTAATT	104	1000
1101286	6612	6631	51138	51157	CAAATATTTATACAGAACAG	78	1001
1101287	6614	6633	51140	51159	TTCAAATATTTATACAGAAC	70	1002
1101288	6615	6634	51141	51160	TTTCAAATATTTATACAGAA	42	1003
1101289	6616	6635	51142	51161	ATTTCAAATATTTATACAGA	87	1004
1101290	6618	6637	51144	51163	GAATTTCAAATATTTATACA	97	1005
1101291	6621	6640	51147	51166	CTTGAATTTCAAATATTTAT	94	1006

1101292	6636	6655	51162	51181	CAGATATTTTCTGTACTTGA	32	1007
1101293	6645	6664	51171	51190	TTTTTGTTTCAGATATTTTC	82	1008
1101295	6661	6680	51187	51206	GGCCAAACAACAATGCTTTT	72	1009
1101297	6664	6683	51190	51209	CATGGCCAAACAACAATGCT	83	1010
1101298	6665	6684	51191	51210	TCATGGCCAAACAACAATGC	80	1011
1101299	6667	6686	51193	51212	TATCATGGCCAAACAACAAT	76	1012
1101300	6674	6693	51200	51219	GCACTTGTATCATGGCCAAA	50	1013
1101301	6675	6694	51201	51220	TGCACTTGTATCATGGCCAA	64	1014
1101302	6750	6769	51276	51295	AGCAAATGAACTTAACGAGG	32	1015
1101303	6756	6775	51282	51301	AATAACAGCAAATGAACTTA	64	1016
1101304	6762	6781	51288	51307	GTGTGTAATAACAGCAAATG	52	1017
1101305	6764	6783	51290	51309	GTGTGTGTAATAACAGCAAA	81	1018
1101306	6765	6784	51291	51310	TGTGTGTGTAATAACAGCAA	65	1019
1101307	6798	6817	51324	51343	GCCCGGCTTTTCTAACGACC	77	1020
1101308	6839	6858	51365	51384	CACACTAACAACAGAATCCT	75	1021
1101309	6841	6860	51367	51386	TCCACACTAACAACAGAATC	94	1022
1101310	6842	6861	51368	51387	ATCCACACTAACAACAGAAT	72	1023
1101311	6844	6863	51370	51389	ACATCCACACTAACAACAGA	57	1024
1101312	6845	6864	51371	51390	AACATCCACACTAACAACAG	70	1025
1101313	6846	6865	51372	51391	GAACATCCACACTAACAACA	73	1026
1101314	6848	6867	51374	51393	TTGAACATCCACACTAACAA	73	1027
1101315	6851	6870	51377	51396	TCATTGAACATCCACACTAA	62	1028
1101316	6852	6871	51378	51397	CTCATTGAACATCCACACTA	70	1029
1101317	6853	6872	51379	51398	ACTCATTGAACATCCACACT	69	1030
1101318	6854	6873	51380	51399	AACTCATTGAACATCCACAC	67	1031
1101319	6860	6879	51386	51405	AAATACAACTCATTGAACAT	66	1032
1101320	6861	6880	51387	51406	AAAATACAACTCATTGAACA	88	1033
1101321	6862	6881	51388	51407	TAAAATACAACTCATTGAAC	81	1034
1101322	6863	6882	51389	51408	TTAAAATACAACTCATTGAA	102	1035
1101323	6865	6884	51391	51410	ATTTAAAATACAACTCATTG	73	1036
1101324	6867	6886	51393	51412	ATATTTAAAATACAACTCAT	101	1037
1101325	6868	6887	51394	51413	GATATTTAAAATACAACTCA	38	1038
1101326	6869	6888	51395	51414	TGATATTTAAAATACAACTC	83	1039
1101327	6870	6889	51396	51415	TTGATATTTAAAATACAACT	77	1040
1101328	6871	6890	51397	51416	TTTGATATTTAAAATACAAC	77	1041
1101329	6880	6899	51406	51425	TTAATAATCTTTGATATTTA	129	1042
1101331	6887	6906	51413	51432	TCTTTATTTAATAATCTTTG	80	1043
1101333	6891	6910	51417	51436	ATTATCTTTATTTAATAATC	91	1044
1101334	6895	6914	51421	51440	AAACATTATCTTTATTTAAT	79	1045
1101335	6902	6921	51428	51447	GAAAAGCAAACATTATCTTT	99	1046
1101336	90	109	N/A	N/A	AAAGTGAGCCTTCTTGTTTC	57	1047
1101337	92	111	N/A	N/A	ACAAAGTGAGCCTTCTTGTT	54	1048
1101338	93	112	N/A	N/A	CACAAAGTGAGCCTTCTTGT	62	1049

1101339	94	113	13163	13182	GCACAAAGTGAGCCTTCTTG	11	1050
1101340	95	114	13164	13183	AGCACAAAGTGAGCCTTCTT	35	1051
1101341	96	115	13165	13184	GAGCACAAAGTGAGCCTTCT	102	1052
1101342	97	116	13166	13185	TGAGCACAAAGTGAGCCTTC	75	1053
1101343	98	117	13167	13186	TTGAGCACAAAGTGAGCCTT	60	1054
1101344	100	119	13169	13188	TGTTGAGCACAAAGTGAGCC	45	1055
1101345	116	135	13185	13204	TAAGTTATTCAGGCAATGTT	35	1056
1101346	118	137	13187	13206	AATAAGTTATTCAGGCAATG	34	1057
1101347	136	155	13205	13224	CTAAAATATTCTCCTTGCAA	51	1058
1101348	137	156	13206	13225	GCTAAAATATTCTCCTTGCA	33	1059
1101349	138	157	13207	13226	GGCTAAAATATTCTCCTTGC	12	1060
1101350	152	171	13221	13240	GGATAATTCCACAGGGCTAA	13	1061
1101351	153	172	13222	13241	AGGATAATTCCACAGGGCTA	9	1062
1101352	154	173	13223	13242	GAGGATAATTCCACAGGGCT	12	1063
1101353	155	174	13224	13243	TGAGGATAATTCCACAGGGC	21	1064
1101354	156	175	13225	13244	TTGAGGATAATTCCACAGGG	21	1065
1101355	157	176	13226	13245	ATTGAGGATAATTCCACAGG	46	1066
1101356	158	177	13227	13246	AATTGAGGATAATTCCACAG	53	1067
1101357	183	202	13252	13271	TCTCCTCCTCATCCAGCTGA	54	1068
1101358	184	203	13253	13272	CTCTCCTCCTCATCCAGCTG	83	1069
1101359	186	205	13255	13274	TCCTCTCCTCCTCATCCAGC	28	1070
1101360	187	206	13256	13275	ATCCTCTCCTCCTCATCCAG	44	1071
1101361	189	208	13258	13277	TCATCCTCTCCTCCTCATCC	41	1072
1101362	193	212	13262	13281	ATTCTCATCCTCTCCTCCTC	37	1073
1101363	194	213	13263	13282	CATTCTCATCCTCTCCTCCT	49	1074
1101364	197	216	13266	13285	TGCCATTCTCATCCTCTCCT	15	1075
1101365	198	217	13267	13286	CTGCCATTCTCATCCTCTCC	26	1076
1101367	211	230	13280	13299	GTAACTCCTCCTTCTGCCAT	31	1077
1101369	214	233	13283	13302	CTAGTAACTCCTCCTTCTGC	35	1078
1101370	215	234	13284	13303	ACTAGTAACTCCTCCTTCTG	22	1079
1101371	217	236	13286	13305	TCACTAGTAACTCCTCCTTC	75	1080
1101372	218	237	13287	13306	TTCACTAGTAACTCCTCCTT	69	1081
1101373	220	239	13289	13308	TCTTCACTAGTAACTCCTCC	67	1082
1101374	225	244	13294	13313	GATAATCTTCACTAGTAACT	66	1083
1101375	227	246	13296	13315	GCGATAATCTTCACTAGTAA	35	1084
1101376	228	247	13297	13316	TGCGATAATCTTCACTAGTA	60	1085
1101377	229	248	13298	13317	GTGCGATAATCTTCACTAGT	97	1086
1101378	230	249	13299	13318	CGTGCGATAATCTTCACTAG	74	1087
1101379	248	267	N/A	N/A	AGAAGGCTGCTGTAAAAACG	44	1088
1101380	249	268	N/A	N/A	CAGAAGGCTGCTGTAAAAAC	51	1089
1101381	251	270	N/A	N/A	TCCAGAAGGCTGCTGTAAAA	51	1090
1101382	258	277	13863	13882	CCATATTTCCAGAAGGCTGC	35	1091
1101383	259	278	13864	13883	TCCATATTTCCAGAAGGCTG	21	1092

1101384	260	279	13865	13884	ATCCATATTTCCAGAAGGCT	15	1093
1101385	261	280	13866	13885	CATCCATATTTCCAGAAGGC	26	1094
1101386	262	281	13867	13886	TCATCCATATTTCCAGAAGG	56	1095
1101387	263	282	13868	13887	GTCATCCATATTTCCAGAAG	31	1096
1101388	266	285	13871	13890	ACTGTCATCCATATTTCCAG	23	1097
1101389	267	286	13872	13891	CACTGTCATCCATATTTCCA	61	1098
1101390	270	289	13875	13894	AACCACTGTCATCCATATTT	56	1099
1101391	275	294	13880	13899	GAAAAAACCACTGTCATCCA	40	1100
1101392	276	295	13881	13900	AGAAAAAACCACTGTCATCC	60	1101
1101393	278	297	13883	13902	AGAGAAAAAACCACTGTCAT	66	1102
1101394	279	298	13884	13903	TAGAGAAAAAACCACTGTCA	64	1103
1101395	281	300	13886	13905	AATAGAGAAAAAACCACTGT	83	1104
1101396	282	301	13887	13906	GAATAGAGAAAAAACCACTG	62	1105
1101397	283	302	13888	13907	TGAATAGAGAAAAAACCACT	68	1106
1101398	284	303	13889	13908	CTGAATAGAGAAAAAACCAC	115	1107
1101405	291	310	N/A	N/A	TTATAACCTGAATAGAGAAA	111	1108
1101406	293	312	N/A	N/A	GCTTATAACCTGAATAGAGA	39	1109
1101407	294	313	N/A	N/A	TGCTTATAACCTGAATAGAG	41	1110
1101408	295	314	N/A	N/A	TTGCTTATAACCTGAATAGA	57	1111
1101409	296	315	N/A	N/A	ATTGCTTATAACCTGAATAG	63	1112
1101410	298	317	N/A	N/A	GCATTGCTTATAACCTGAAT	43	1113
1101411	299	318	N/A	N/A	GGCATTGCTTATAACCTGAA	11	1114
1101412	N/A	N/A	51448	51467	CACAAATTCAAAAGGAAATA	109	1115
1101413	N/A	N/A	51449	51468	ACACAAATTCAAAAGGAAAT	83	1116
1101414	N/A	N/A	51451	51470	AAACACAAATTCAAAAGGAA	92	1117
1101415	N/A	N/A	51452	51471	TAAACACAAATTCAAAAGGA	91	1118
1101416	N/A	N/A	51459	51478	TTAACAATAAACACAAATTC	79	1119
1101417	N/A	N/A	51464	51483	ATGAATTAACAATAAACACA	155	1120
1101418	N/A	N/A	51465	51484	TATGAATTAACAATAAACAC	101	1121
1101419	N/A	N/A	51466	51485	CTATGAATTAACAATAAACA	107	1122
1101420	N/A	N/A	51469	51488	TAGCTATGAATTAACAATAA	99	1123
1101421	N/A	N/A	51471	51490	AATAGCTATGAATTAACAAT	70	1124
1101422	N/A	N/A	51857	51876	AATAGAATATCAATGGACTG	65	1125
1101423	N/A	N/A	51860	51879	TGGAATAGAATATCAATGGA	54	1126
1101424	N/A	N/A	51862	51881	GCTGGAATAGAATATCAATG	52	1127
1101425	N/A	N/A	51943	51962	TCAAATAAAAATTTGGAATT	108	1128
1101426	N/A	N/A	51944	51963	TTCAAATAAAAATTTGGAAT	82	1129
1101427	N/A	N/A	52274	52293	TCCTCAATCAGTCTAGGTGG	89	1130
1101428	N/A	N/A	52275	52294	TTCCTCAATCAGTCTAGGTG	92	1131
1101429	N/A	N/A	52281	52300	AATATATTCCTCAATCAGTC	114	1132
1101430	N/A	N/A	52282	52301	CAATATATTCCTCAATCAGT	90	1133
1101431	N/A	N/A	52283	52302	ACAATATATTCCTCAATCAG	112	1134
1101432	N/A	N/A	52338	52357	GTGCCCAATCCTAATTAAAG	130	1135

1101433	N/A	N/A	52339	52358	TGTGCCCAATCCTAATTAAA	97	1136
1101434	N/A	N/A	52352	52371	ATGTTTCAAAATTTGTGCCC	64	1137
1101435	N/A	N/A	52354	52373	TTATGTTTCAAAATTTGTGC	89	1138
1101436	N/A	N/A	52355	52374	ATTATGTTTCAAAATTTGTG	81	1139
1101437	N/A	N/A	53333	53352	ACCCTAATACAAGAGACTCT	110	1140
1101439	N/A	N/A	53336	53355	TCTACCCTAATACAAGAGAC	100	1141
1101441	N/A	N/A	53779	53798	CCATGTAGTGACATGTGGCT	87	1142
1101442	N/A	N/A	53929	53948	TTTTGGAAAAAATGGATCTG	93	1143
1101443	N/A	N/A	53930	53949	CTTTTGGAAAAAATGGATCT	88	1144
1101444	N/A	N/A	53931	53950	GCTTTTGGAAAAAATGGATC	82	1145
1101445	N/A	N/A	53944	53963	GAATTCAAACACAGCTTTTG	90	1146
1101446	N/A	N/A	53948	53967	TGCAGAATTCAAACACAGCT	82	1147
1101447	N/A	N/A	53951	53970	CTGTGCAGAATTCAAACACA	66	1148
1101574	N/A	N/A	3683	3702	GCCCATACTCCCTCCCGGCT	106	1149
1101575	N/A	N/A	3690	3709	CGGCCCCGCCCATACTCCCT	101	1150
1101576	N/A	N/A	3740	3759	AGAAGCAAACCCACTGGGCG	96	1151
1101577	N/A	N/A	3885	3904	GAAAAGTTAATTCTGCCAGG	49	1152
1101578	N/A	N/A	3948	3967	ACAAGACCCCAAAGATCTAC	71	1153
1101579	N/A	N/A	4012	4031	AGTGGGCGAGCCAAGGTCTC	87	1154
1101580	N/A	N/A	4093	4112	GTAATAAAAACTCTTGTGAC	61	1155
1101581	N/A	N/A	4109	4128	CAAACCCAAACATCCCGTAA	135	1156
1101583	N/A	N/A	4113	4132	AAACCAAACCCAAACATCCC	80	1157
1101585	N/A	N/A	4128	4147	TGGGAGTACCAAAAGAAACC	71	1158
1101586	N/A	N/A	4165	4184	TACCTAAAAACAAAGCTGGC	86	1159
1101587	N/A	N/A	4166	4185	ATACCTAAAAACAAAGCTGG	69	1160
1101588	N/A	N/A	4168	4187	TAATACCTAAAAACAAAGCT	90	1161
1101589	N/A	N/A	4170	4189	CCTAATACCTAAAAACAAAG	102	1162
1101590	N/A	N/A	4171	4190	TCCTAATACCTAAAAACAAA	95	1163
1101591	N/A	N/A	4172	4191	CTCCTAATACCTAAAAACAA	81	1164
1101592	N/A	N/A	4173	4192	ACTCCTAATACCTAAAAACA	85	1165
1101593	N/A	N/A	4174	4193	CACTCCTAATACCTAAAAAC	83	1166
1101594	N/A	N/A	4175	4194	CCACTCCTAATACCTAAAAA	117	1167
1101595	N/A	N/A	4180	4199	CCAGTCCACTCCTAATACCT	63	1168
1101596	N/A	N/A	4194	4213	ACAACAAAATCATCCCAGTC	77	1169
1101597	N/A	N/A	4195	4214	TACAACAAAATCATCCCAGT	71	1170
1101598	N/A	N/A	4254	4273	AACAGTATCTTCAAGTGCAT	53	1171
1101599	N/A	N/A	4255	4274	AAACAGTATCTTCAAGTGCA	52	1172
1101600	N/A	N/A	4277	4296	GAGGAGTTTCTTTACATATC	13	1173
1101601	N/A	N/A	4357	4376	AACATGATACCATGTGCCAA	27	1174
1101602	N/A	N/A	4375	4394	AACACGAAACTATTATGAAA	88	1175
1101603	N/A	N/A	4415	4434	TCCTCCTATTAAATAACAGC	62	1176
1101604	N/A	N/A	4421	4440	CTTTGCTCCTCCTATTAAAT	55	1177
1101605	N/A	N/A	4459	4478	TAAATGATCATTTATAAGTA	100	1178

1101606	N/A	N/A	4481	4500	TGTGAATTTTAAATGTCTGG	30	1179
1101607	N/A	N/A	4482	4501	GTGTGAATTTTAAATGTCTG	19	1180
1101608	N/A	N/A	4483	4502	TGTGTGAATTTTAAATGTCT	45	1181
1101609	N/A	N/A	4484	4503	GTGTGTGAATTTTAAATGTC	35	1182
1101610	N/A	N/A	4728	4747	TCTCCCAAAAACATTACCTG	179	1183
1101611	N/A	N/A	4732	4751	CGTCTCTCCCAAAAACATTA	88	1184
1101612	N/A	N/A	4857	4876	GTACTTAACAATTTGTTCCA	46	1185
1101613	N/A	N/A	4858	4877	TGTACTTAACAATTTGTTCC	47	1186
1101614	N/A	N/A	4864	4883	AAGCATTGTACTTAACAATT	55	1187
1101615	N/A	N/A	4884	4903	GAGATGTTTTCTACAATGAA	26	1188
1101616	N/A	N/A	4903	4922	GCCTATTTCAAAAGTTTCCG	42	1189
1101617	N/A	N/A	4904	4923	AGCCTATTTCAAAAGTTTCC	59	1190
1101619	N/A	N/A	4949	4968	TAGTGACAACTATACGACTG	53	1191
1101621	N/A	N/A	5009	5028	CCAAGCAACCAAATCTCTAT	67	1192
1101622	N/A	N/A	5351	5370	ATAACAAAAATATGGCCGGG	91	1193
1101623	N/A	N/A	5352	5371	AATAACAAAAATATGGCCGG	91	1194
1101624	N/A	N/A	5353	5372	TAATAACAAAAATATGGCCG	101	1195
1101625	N/A	N/A	5354	5373	TTAATAACAAAAATATGGCC	85	1196
1101626	N/A	N/A	5355	5374	ATTAATAACAAAAATATGGC	163	1197
1101627	N/A	N/A	5356	5375	AATTAATAACAAAAATATGG	83	1198
1101628	N/A	N/A	5363	5382	CTTTGAAAATTAATAACAAA	115	1199
1101629	N/A	N/A	5365	5384	GCCTTTGAAAATTAATAACA	85	1200
1101630	N/A	N/A	5378	5397	GTCCCACACCAAAGCCTTTG	73	1201
1101631	N/A	N/A	5452	5471	ATATTGTTAAAAATCTTGTC	72	1202
1101632	N/A	N/A	5454	5473	CAATATTGTTAAAAATCTTG	79	1203
1101633	N/A	N/A	5959	5978	AAAAACTAAATTGTTGAATC	98	1204
1101634	N/A	N/A	5962	5981	CCAAAAAACTAAATTGTTGA	77	1205
1101635	N/A	N/A	5964	5983	GCCCAAAAAACTAAATTGTT	98	1206
1101636	N/A	N/A	5965	5984	CGCCCAAAAAACTAAATTGT	87	1207
1101637	N/A	N/A	6050	6069	CACAGTAAGCCCAAACATTC	85	1208
1101638	N/A	N/A	6102	6121	AGCAAGGGTTAAAGGTATAT	68	1209
1101639	N/A	N/A	6121	6140	CTCTCCAAACCCAGGACCTA	115	1210
1101640	N/A	N/A	6147	6166	CTTTAGGGCCAAAGTTGGTT	70	1211
1101641	N/A	N/A	6156	6175	ACACAGCTTCTTTAGGGCCA	56	1212
1101642	N/A	N/A	6212	6231	CCAAGGTTCCAAGAGGAAAT	60	1213
1101643	N/A	N/A	6221	6240	AAGAGGAAACCAAGGTTCCA	94	1214
1101644	N/A	N/A	6247	6266	AAGGGTACTCAAAGTGACTA	69	1215
1101645	N/A	N/A	6264	6283	TACATTCTAACTTAATAAAG	93	1216
1101646	N/A	N/A	6269	6288	GTTTTTACATTCTAACTTAA	65	1217
1101647	N/A	N/A	6274	6293	AAACTGTTTTTACATTCTAA	64	1218
1101648	N/A	N/A	6275	6294	GAAACTGTTTTTACATTCTA	58	1219
1101649	N/A	N/A	6348	6367	GCCCCATTCAAATATTTATT	137	1220
1101650	N/A	N/A	6558	6577	TCCATTCAAATATATACATT	74	1221

1101651	N/A	N/A	6561	6580	TTATCCATTCAAATATATAC	90	1222
1101652	N/A	N/A	6565	6584	CTCTTTATCCATTCAAATAT	70	1223
1101653	N/A	N/A	6566	6585	TCTCTTTATCCATTCAAATA	79	1224
1101655	N/A	N/A	6593	6612	CATATATATCTCAGAAACTC	62	1225
1101657	N/A	N/A	6597	6616	GCACCATATATATCTCAGAA	15	1226
1101658	N/A	N/A	6598	6617	AGCACCATATATATCTCAGA	25	1227
1101659	N/A	N/A	6599	6618	CAGCACCATATATATCTCAG	21	1228
1101660	N/A	N/A	6601	6620	AACAGCACCATATATATCTC	54	1229
1101661	N/A	N/A	6610	6629	CTTTAGATAAACAGCACCAT	66	1230
1101662	N/A	N/A	6614	6633	TTTACTTTAGATAAACAGCA	56	1231
1101663	N/A	N/A	6639	6658	CCTTAAAATATTTACAGAAA	78	1232
1101664	N/A	N/A	6648	6667	CCTGCAAAGCCTTAAAATAT	92	1233
1101665	N/A	N/A	6667	6686	TGACAGAGACTACAGCTGGC	85	1234
1101666	N/A	N/A	6698	6717	GTTGGGAAAAACATGCACAA	43	1235
1101667	N/A	N/A	6700	6719	TGGTTGGGAAAAACATGCAC	34	1236
1101668	N/A	N/A	6716	6735	ACTTTACATTTTTACATGGT	25	1237
1101669	N/A	N/A	6731	6750	AGTAGCTAAGAATGCACTTT	74	1238
1101670	N/A	N/A	6754	6773	ATGGGCCAAATTCAACCTGC	90	1239
1101671	N/A	N/A	6824	6843	CAACAAAAATCCAGTAGTGG	68	1240
1101672	N/A	N/A	6825	6844	ACAACAAAAATCCAGTAGTG	68	1241
1101673	N/A	N/A	6842	6861	CAGAACTAAAACAAACAACA	78	1242
1101674	N/A	N/A	6844	6863	ACCAGAACTAAAACAAACAA	92	1243
1101675	N/A	N/A	6845	6864	CACCAGAACTAAAACAAACA	106	1244
1101676	N/A	N/A	6847	6866	GGCACCAGAACTAAAACAAA	67	1245
1101677	N/A	N/A	6851	6870	AGCAGGCACCAGAACTAAAA	74	1246
1101678	N/A	N/A	6903	6922	TAACTGCACCAAGAAACATC	93	1247
1101679	N/A	N/A	6924	6943	GCACCAATACAAATGGCACA	60	1248
1101680	N/A	N/A	6926	6945	AAGCACCAATACAAATGGCA	69	1249
1101681	N/A	N/A	6941	6960	TTTGCATTACATTAAAAGCA	64	1250
1101682	N/A	N/A	6955	6974	GATATTATTACCAGTTTGCA	17	1251
1101683	N/A	N/A	6977	6996	ATGTACAACCCCAGCAAGTT	41	1252
1101684	N/A	N/A	6978	6997	TATGTACAACCCCAGCAAGT	73	1253
1101685	N/A	N/A	6989	7008	TTCAATAATTTTATGTACAA	95	1254
1101686	N/A	N/A	7037	7056	GGGCATAATGAATGCCACAG	75	1255
1101687	N/A	N/A	7062	7081	TGGCTAAAATCCAGCAATCA	68	1256
1101688	N/A	N/A	7093	7112	GGCTTCTCCTAAAGCTCAAA	73	1257
1101689	N/A	N/A	7110	7129	TCATTTATACAGAATTTGGC	21	1258
1101691	N/A	N/A	7120	7139	GCACTTCAAGTCATTTATAC	57	1259
1101693	N/A	N/A	7304	7323	ACTATCTGCCAGGGAGCCTT	76	1260
1101694	N/A	N/A	7328	7347	GGCAATGGCCAGTACTTCTA	79	1261
1101695	N/A	N/A	7377	7396	TCTCCGAGCCCTTACTATGA	74	1262
1101696	N/A	N/A	7462	7481	AGGTATAAACCTAAGGTGCT	58	1263
1101697	N/A	N/A	7474	7493	ACAACACAAATCAGGTATAA	93	1264

1101698	N/A	N/A	7477	7496	ACTACAACACAAATCAGGTA	80	1265
1101699	N/A	N/A	7479	7498	TAACTACAACACAAATCAGG	73	1266
1101700	N/A	N/A	7485	7504	CACTACTAACTACAACACAA	70	1267
1101701	N/A	N/A	7486	7505	ACACTACTAACTACAACACA	91	1268
1101702	N/A	N/A	7491	7510	CAGAGACACTACTAACTACA	66	1269
1101703	N/A	N/A	7502	7521	GTTCAAATTACCAGAGACAC	75	1270
1101704	N/A	N/A	7504	7523	TAGTTCAAATTACCAGAGAC	60	1271
1101705	N/A	N/A	7505	7524	CTAGTTCAAATTACCAGAGA	66	1272
1101706	N/A	N/A	7508	7527	AAACTAGTTCAAATTACCAG	84	1273
1101707	N/A	N/A	7521	7540	CAAGACCAACCTGAAACTAG	70	1274
1101708	N/A	N/A	7526	7545	GTTTTCAAGACCAACCTGAA	108	1275
1101709	N/A	N/A	7549	7568	TCATTTACCCCCAACCTCCC	78	1276
1101710	N/A	N/A	7552	7571	AAATCATTTACCCCCAACCT	81	1277
1101711	N/A	N/A	7556	7575	TACCAAATCATTTACCCCCA	53	1278
1101712	N/A	N/A	7558	7577	GCTACCAAATCATTTACCCC	82	1279
1101713	N/A	N/A	7559	7578	TGCTACCAAATCATTTACCC	80	1280
1101714	N/A	N/A	7562	7581	AACTGCTACCAAATCATTTA	53	1281
1101715	N/A	N/A	7600	7619	GCAGTTCTACAAAGATAATG	46	1282
1101716	N/A	N/A	8424	8443	ATTGAAATCTCATGATTTGG	92	1283
1101717	N/A	N/A	8425	8444	TATTGAAATCTCATGATTTG	86	1284
1101718	N/A	N/A	8447	8466	TGCCATAATCAAAGTTCAGC	29	1285
1101719	N/A	N/A	8449	8468	TTTGCCATAATCAAAGTTCA	69	1286
1101720	N/A	N/A	8453	8472	TCACTTTGCCATAATCAAAG	52	1287
1101721	N/A	N/A	8455	8474	GTTCACTTTGCCATAATCAA	26	1288
1101722	N/A	N/A	8474	8493	AGCTTTAATCAAAGCAGAAG	86	1289
1101723	N/A	N/A	8477	8496	TCAAGCTTTAATCAAAGCAG	106	1290
1101724	N/A	N/A	8504	8523	TCAAACTATCCCCAGCCACC	107	1291
1101725	N/A	N/A	8508	8527	TATCTCAAACTATCCCCAGC	108	1292
1101727	N/A	N/A	8510	8529	CTTATCTCAAACTATCCCCA	123	1293
1101729	N/A	N/A	8514	8533	TGCCCTTATCTCAAACTATC	104	1294
1101730	N/A	N/A	8520	8539	CTGCCTTGCCCTTATCTCAA	79	1295
1101731	N/A	N/A	8531	8550	TATGCATTTTCCTGCCTTGC	71	1296
1101732	N/A	N/A	8571	8590	ACCAAAAGAATTGTACAATG	85	1297
1101733	N/A	N/A	8573	8592	GGACCAAAAGAATTGTACAA	106	1298
1101734	N/A	N/A	8578	8597	CACATGGACCAAAAGAATTG	114	1299
1101735	N/A	N/A	8591	8610	ACGGATCAAATTCCACATGG	51	1300
1101736	N/A	N/A	8785	8804	TGGTTCATACTATAATCTCA	26	1301
1101737	N/A	N/A	8823	8842	TCAGTACAAATTTAAAAATC	81	1302
1101738	N/A	N/A	8826	8845	TGTTCAGTACAAATTTAAAA	76	1303
1101739	N/A	N/A	8831	8850	CAAACTGTTCAGTACAAATT	71	1304
1101740	N/A	N/A	8837	8856	AAAGGACAAACTGTTCAGTA	35	1305
1101741	N/A	N/A	8860	8879	TTCTAATATGATTTAATGGA	94	1306
1101742	N/A	N/A	8861	8880	CTTCTAATATGATTTAATGG	62	1307

1101743	N/A	N/A	8882	8901	CAGGAAATATCAAGTTCTGT	47	1308
1101744	N/A	N/A	8883	8902	ACAGGAAATATCAAGTTCTG	81	1309
1101745	N/A	N/A	8903	8922	CAAAGAAAAACTGTATTGCT	53	1310
1101746	N/A	N/A	8917	8936	AAATCAAACTTCATCAAAGA	90	1311
1101747	N/A	N/A	8918	8937	GAAATCAAACTTCATCAAAG	52	1312
1101748	N/A	N/A	8919	8938	TGAAATCAAACTTCATCAAA	86	1313
1101749	N/A	N/A	8922	8941	ACTTGAAATCAAACTTCATC	57	1314
1101750	N/A	N/A	8947	8966	TAGCTTTAAATTATGAAAAA	97	1315
1101751	N/A	N/A	8948	8967	ATAGCTTTAAATTATGAAAA	64	1316
1101752	N/A	N/A	8950	8969	AAATAGCTTTAAATTATGAA	99	1317
1101753	N/A	N/A	8959	8978	CTCTATAAAAAATAGCTTTA	103	1318
1101754	N/A	N/A	8973	8992	TTGATTAAAATTCTCTCTAT	97	1319
1101755	N/A	N/A	8986	9005	GACATCCAAATATTTGATTA	33	1320
1101756	N/A	N/A	8989	9008	AGTGACATCCAAATATTTGA	49	1321
1101757	N/A	N/A	9010	9029	CTTAATACCATATATAGCAA	71	1322
1101758	N/A	N/A	9012	9031	TACTTAATACCATATATAGC	73	1323
1101759	N/A	N/A	9013	9032	ATACTTAATACCATATATAG	115	1324
1101760	N/A	N/A	9023	9042	TATGGTCACCATACTTAATA	66	1325
1101761	N/A	N/A	9033	9052	GTTTACAAACTATGGTCACC	78	1326
1101763	N/A	N/A	9035	9054	GAGTTTACAAACTATGGTCA	58	1327
1101765	N/A	N/A	9064	9083	CACAAATTTCCTGTCTTGCT	59	1328
1101766	N/A	N/A	9068	9087	CTAACACAAATTTCCTGTCT	62	1329
1101767	N/A	N/A	9071	9090	TTGCTAACACAAATTTCCTG	73	1330
1101768	N/A	N/A	9073	9092	CTTTGCTAACACAAATTTCC	77	1331
1101769	N/A	N/A	9083	9102	AGAAAAAAGCCTTTGCTAAC	95	1332
1101770	N/A	N/A	9101	9120	TAAAAAATTCAAACAGTAAG	86	1333
1101771	N/A	N/A	9319	9338	TCAGGCAAAACTCATTTATG	44	1334
1101772	N/A	N/A	9340	9359	TCCAGTCACAAAAGCTCAAA	65	1335
1101773	N/A	N/A	9341	9360	TTCCAGTCACAAAAGCTCAA	92	1336
1101774	N/A	N/A	9389	9408	ATGGTAAACTAAAGAGGACA	88	1337
1101775	N/A	N/A	9392	9411	ACAATGGTAAACTAAAGAGG	63	1338
1101776	N/A	N/A	9400	9419	TTTCTCAAACAATGGTAAAC	50	1339
1101777	N/A	N/A	9406	9425	GATAAATTTCTCAAACAATG	102	1340
1101778	N/A	N/A	9447	9466	AATTAACAATAATTAACAGT	79	1341
1101779	N/A	N/A	9450	9469	GTTAATTAACAATAATTAAC	103	1342
1101780	N/A	N/A	9470	9489	ATGAATTAACTACAACAGTA	118	1343
1101781	N/A	N/A	9500	9519	CTCACAAAAGAATACTAGAT	61	1344
1101782	N/A	N/A	9507	9526	GTGTTTACTCACAAAAGAAT	65	1345
1101783	N/A	N/A	9552	9571	GAAACGACCCAAATGGATAG	75	1346
1101784	N/A	N/A	9554	9573	TGGAAACGACCCAAATGGAT	80	1347
1101785	N/A	N/A	9585	9604	ATAGCATTACTATTTGTAAT	68	1348
1101786	N/A	N/A	9597	9616	ATAGCATTACAGATAGCATT	40	1349
1101787	N/A	N/A	9610	9629	GTAGTAATACAAAATAGCAT	85	1350

1101788	N/A	N/A	9625	9644	ATAGCATTACTATTTGTAGT	68	1351
1101789	N/A	N/A	9746	9765	ATCTCCTATGATCTAGCAAT	68	1352
1101790	N/A	N/A	9761	9780	AAGCTTAATATATACATCTC	81	1353
1101791	N/A	N/A	9763	9782	TAAAGCTTAATATATACATC	115	1354
1101792	N/A	N/A	9788	9807	ACTAATAATTATGTAATGCA	98	1355
1101793	N/A	N/A	9790	9809	TAACTAATAATTATGTAATG	126	1356
1101794	N/A	N/A	9791	9810	ATAACTAATAATTATGTAAT	84	1357
1101795	N/A	N/A	9792	9811	AATAACTAATAATTATGTAA	109	1358
1101796	N/A	N/A	9797	9816	CCAATAATAACTAATAATTA	88	1359
1101797	N/A	N/A	9798	9817	ACCAATAATAACTAATAATT	111	1360
1101799	N/A	N/A	9806	9825	TTGGTATAACCAATAATAAC	85	1361
1101801	N/A	N/A	9882	9901	CACAAACTCTAAAATGGCTA	72	1362
1101802	N/A	N/A	9997	10016	GGCAAGACAAACAAGCACTT	77	1363
1101803	N/A	N/A	10199	10218	CTTGAGCCCCAAAAAGGTCG	93	1364
1101804	N/A	N/A	10409	10428	TGAAAAATAGCCAAGGCTGG	96	1365
1101805	N/A	N/A	10424	10443	CTACTTATATCCTTTTGAAA	65	1366
1101806	N/A	N/A	10439	10458	GGATATACAGATGTTCTACT	25	1367
1101807	N/A	N/A	10441	10460	AGGGATATACAGATGTTCTA	39	1368
1101808	N/A	N/A	10443	10462	GAAGGGATATACAGATGTTC	27	1369
1101809	N/A	N/A	10463	10482	TACTGAATAATATGCAAATT	99	1370
1101810	N/A	N/A	10468	10487	ACTCTTACTGAATAATATGC	75	1371
1101811	N/A	N/A	10489	10508	TATTTCTACTACCAGAGTGC	38	1372
1101812	N/A	N/A	10505	10524	CTTTCTCCTCCTTATATATT	67	1373
1101813	N/A	N/A	10605	10624	AAGTTTATCTTCAACTTTTC	59	1374
1101814	N/A	N/A	10606	10625	TAAGTTTATCTTCAACTTTT	101	1375
1101815	N/A	N/A	10676	10695	GTGAAAAAAATATGGGTTAT	55	1376
1101816	N/A	N/A	10677	10696	GGTGAAAAAAATATGGGTTA	37	1377
1101817	N/A	N/A	10678	10697	TGGTGAAAAAAATATGGGTT	21	1378
1101818	N/A	N/A	10679	10698	CTGGTGAAAAAAATATGGGT	57	1379
1101819	N/A	N/A	10681	10700	AGCTGGTGAAAAAAATATGG	90	1380
1101820	N/A	N/A	10683	10702	TCAGCTGGTGAAAAAAATAT	93	1381
1101821	N/A	N/A	10694	10713	AGGAGCAAAATTCAGCTGGT	49	1382
1101822	N/A	N/A	10745	10764	AAAGAGAACCACCTTGCAAG	87	1383
1101823	N/A	N/A	10747	10766	CTAAAGAGAACCACCTTGCA	68	1384
1101824	N/A	N/A	10809	10828	TTCCTTAACCCAACCTATCT	107	1385
1101825	N/A	N/A	10810	10829	ATTCCTTAACCCAACCTATC	80	1386
1101826	N/A	N/A	10815	10834	GGTCTATTCCTTAACCCAAC	53	1387
1101827	N/A	N/A	10816	10835	AGGTCTATTCCTTAACCCAA	77	1388
1101828	N/A	N/A	10817	10836	AAGGTCTATTCCTTAACCCA	42	1389
1101829	N/A	N/A	10833	10852	TCTCTCTTTCCCCAATAAGG	75	1390
1101830	N/A	N/A	10872	10891	AGAACATTTCCTTCTCCTGC	66	1391
1101831	N/A	N/A	11044	11063	TGAATCCAAGTCCAGGGTGC	79	1392
1101832	N/A	N/A	11071	11090	GGGCAGTTTCTCACACAACT	48	1393

1101833	N/A	N/A	11185	11204	CCTGGACAAGCCAGCAAGAG	110	1394
1101835	N/A	N/A	11215	11234	GAACTGTCCCAAACAACCCT	66	1395
1101837	N/A	N/A	11258	11277	GGAACTCTACAGATAATGTA	66	1396
1101838	N/A	N/A	11303	11322	GTTCCATGTTAAAACTTGCA	146	1397
1101839	N/A	N/A	11308	11327	ATTCTGTTCCATGTTAAAAC	103	1398
1101840	N/A	N/A	11317	11336	GTGAGAAAAATTCTGTTCCA	55	1399
1101841	N/A	N/A	11320	11339	CAGGTGAGAAAAATTCTGTT	126	1400
1101842	N/A	N/A	11370	11389	CACACAATCTAAATGCTTGT	102	1401
1101843	N/A	N/A	11703	11722	CATTTATTCTTTTAACATGA	86	1402
1101844	N/A	N/A	11707	11726	AGAACATTTATTCTTTTAAC	106	1403
1101845	N/A	N/A	11711	11730	CCCTAGAACATTTATTCTTT	88	1404
1101846	N/A	N/A	11870	11889	GAAAGGAAATTTTAGTCCCT	48	1405
1101847	N/A	N/A	11879	11898	ACTAATGGTGAAAGGAAATT	89	1406
1101848	N/A	N/A	11887	11906	AGTAAATTACTAATGGTGAA	51	1407
1101849	N/A	N/A	11888	11907	CAGTAAATTACTAATGGTGA	63	1408
1101850	N/A	N/A	11889	11908	ACAGTAAATTACTAATGGTG	59	1409
1101851	N/A	N/A	11890	11909	TACAGTAAATTACTAATGGT	86	1410
1101852	N/A	N/A	11925	11944	TTCAGTACCTAAAATAAGTT	86	1411
1101853	N/A	N/A	11933	11952	CCCTCATTTTCAGTACCTAA	36	1412
1101854	N/A	N/A	11951	11970	GTATAAAACATTTAGTCTCC	49	1413
1101855	N/A	N/A	11952	11971	TGTATAAAACATTTAGTCTC	70	1414
1101856	N/A	N/A	11953	11972	CTGTATAAAACATTTAGTCT	82	1415
1101857	N/A	N/A	11954	11973	ACTGTATAAAACATTTAGTC	78	1416
1101858	N/A	N/A	11977	11996	AATCTCATATTTTACTAAAA	127	1417
1101859	N/A	N/A	11988	12007	CAAATGCATCAAATCTCATA	59	1418
1101860	N/A	N/A	11997	12016	ATCATCTATCAAATGCATCA	38	1419
1101861	N/A	N/A	12011	12030	TATTTTAAACAAACATCATC	107	1420
1101862	N/A	N/A	12016	12035	AGAATTATTTTAAACAAACA	102	1421
1101863	N/A	N/A	12017	12036	AAGAATTATTTTAAACAAAC	87	1422
1101864	N/A	N/A	12027	12046	TCAAAAATTTAAGAATTATT	80	1423
1101865	N/A	N/A	12028	12047	ATCAAAAATTTAAGAATTAT	130	1424
1101866	N/A	N/A	12030	12049	TGATCAAAAATTTAAGAATT	73	1425
1101867	N/A	N/A	12031	12050	ATGATCAAAAATTTAAGAAT	135	1426
1101868	N/A	N/A	12032	12051	CATGATCAAAAATTTAAGAA	87	1427
1101869	N/A	N/A	12034	12053	TACATGATCAAAAATTTAAG	120	1428
1101871	N/A	N/A	12050	12069	TTAATGAAACTATAATTACA	96	1429
1101873	N/A	N/A	12092	12111	CATGCATTTTCATTTGGTAA	21	1430
1101874	N/A	N/A	12137	12156	TTGAACTGAACTTTCAGCTT	60	1431
1101875	N/A	N/A	12268	12287	ATACGGTTTCACAATGTTAG	42	1432
1101876	N/A	N/A	12770	12789	CTAAATAATTTAATCATTAA	91	1433
1101877	N/A	N/A	12772	12791	CCCTAAATAATTTAATCATT	104	1434
1101878	N/A	N/A	12774	12793	TCCCCTAAATAATTTAATCA	128	1435
1101879	N/A	N/A	12778	12797	CGGCTCCCCTAAATAATTTA	81	1436

1101880	N/A	N/A	13087	13106	ATCTTCCCCTAAATAATTTT	82	1437
1101881	N/A	N/A	13129	13148	AGAAAAAATTAAAATGTGAC	106	1438
1101882	N/A	N/A	13145	13164	TGCTAATATTTCCAAAAGAA	75	1439
1101883	N/A	N/A	13146	13165	TTGCTAATATTTCCAAAAGA	61	1440
1101884	N/A	N/A	13159	13178	AAAGTGAGCCTTCTTGCTAA	74	1441
1101885	N/A	N/A	13328	13347	AGTGAGTTTAAAATCAGTAC	76	1442
1101886	N/A	N/A	13329	13348	TAGTGAGTTTAAAATCAGTA	84	1443
1101887	N/A	N/A	13664	13683	TATCCACATTTTTAAAAGAA	91	1444
1101888	N/A	N/A	13709	13728	CAGTCAGATCCCTATAGGAA	31	1445
1101889	N/A	N/A	13714	13733	TTCACCAGTCAGATCCCTAT	50	1446
1101890	N/A	N/A	13718	13737	ATAATTCACCAGTCAGATCC	59	1447
1101891	N/A	N/A	13720	13739	TTATAATTCACCAGTCAGAT	53	1448
1101892	N/A	N/A	13721	13740	GTTATAATTCACCAGTCAGA	44	1449
1101893	N/A	N/A	13722	13741	AGTTATAATTCACCAGTCAG	46	1450
1101894	N/A	N/A	13723	13742	CAGTTATAATTCACCAGTCA	50	1451
1101895	N/A	N/A	13724	13743	ACAGTTATAATTCACCAGTC	47	1452
1101896	N/A	N/A	13746	13765	TCCCATTTCCAAAGTTAACA	62	1453
1101897	N/A	N/A	13775	13794	GTGCATATTTAAAACAATAT	110	1454
1101898	N/A	N/A	13796	13815	AGGATACAAACTGTCATTAG	141	1455
1101899	N/A	N/A	13799	13818	AGAAGGATACAAACTGTCAT	106	1456
1101900	N/A	N/A	13844	13863	CTGTTAATTTTGACAGGTAG	65	1457
1101901	N/A	N/A	13847	13866	CTGCTGTTAATTTTGACAGG	96	1458
1101902	N/A	N/A	13899	13918	GACTACTTACCTGAATAGAG	84	1459
1101903	N/A	N/A	13904	13923	CTTGTGACTACTTACCTGAA	97	1460
1101904	N/A	N/A	13926	13945	TGTAAGCAACACATAGTACA	98	1461
1101905	N/A	N/A	14015	14034	GAGTATAATCTATACTCTGT	131	1462
1101907	N/A	N/A	14331	14350	TATATAAAAATCTAGTACTC	111	1463
1101909	N/A	N/A	14334	14353	ATCTATATAAAAATCTAGTA	75	1464
1101910	N/A	N/A	14335	14354	TATCTATATAAAAATCTAGT	96	1465
1101911	N/A	N/A	14343	14362	TTCATGTTTATCTATATAAA	82	1466
1101912	N/A	N/A	14350	14369	CAATCCTTTCATGTTTATCT	25	1467
1101913	N/A	N/A	14354	14373	TCTACAATCCTTTCATGTTT	47	1468
1101914	N/A	N/A	14355	14374	TTCTACAATCCTTTCATGTT	43	1469
1101915	N/A	N/A	14356	14375	ATTCTACAATCCTTTCATGT	41	1470
1101916	N/A	N/A	14389	14408	AGGAATTTTTAAATGCCCCA	48	1471
1101917	N/A	N/A	14390	14409	AAGGAATTTTTAAATGCCCC	104	1472
1101918	N/A	N/A	14391	14410	GAAGGAATTTTTAAATGCCC	20	1473
1101919	N/A	N/A	14392	14411	AGAAGGAATTTTTAAATGCC	52	1474
1101920	N/A	N/A	14434	14453	TAAGGTTATTATTAGCATCC	8	1475
1101921	N/A	N/A	14436	14455	ATTAAGGTTATTATTAGCAT	89	1476
1101922	N/A	N/A	14792	14811	CTCAAATTTACCCAACAGAT	96	1477
1101923	N/A	N/A	14796	14815	TTTTCTCAAATTTACCCAAC	77	1478
1101924	N/A	N/A	14830	14849	GGCTGATTTAAAAGGATGGT	48	1479

1101925	N/A	N/A	14831	14850	AGGCTGATTTAAAAGGATGG	57	1480
1101926	N/A	N/A	14834	14853	GGTAGGCTGATTTAAAAGGA	25	1481
1101927	N/A	N/A	14849	14868	AAGGAAATCCAGTCTGGTAG	27	1482
1101928	N/A	N/A	14851	14870	ATAAGGAAATCCAGTCTGGT	78	1483
1101929	N/A	N/A	14864	14883	GCCACAAACCATAATAAGGA	56	1484
1101930	N/A	N/A	14873	14892	AAATCAAAAGCCACAAACCA	73	1485
1101931	N/A	N/A	14895	14914	AGAGCTATACATTAAAAAAA	69	1486
1101932	N/A	N/A	14909	14928	CAAAGAATTCAAAGAGAGCT	89	1487
1101933	N/A	N/A	14914	14933	ACCACCAAAGAATTCAAAGA	119	1488
1101934	N/A	N/A	14918	14937	TATAACCACCAAAGAATTCA	81	1489
1101935	N/A	N/A	14921	14940	ATATATAACCACCAAAGAAT	84	1490
1101936	N/A	N/A	14923	14942	ATATATATAACCACCAAAGA	95	1491
1101937	N/A	N/A	14928	14947	TACATATATATATAACCACC	71	1492
1101938	N/A	N/A	14930	14949	AGTACATATATATATAACCA	96	1493
1101939	N/A	N/A	14949	14968	CAGATAAAAGAATCTTGCGA	84	1494
1101940	N/A	N/A	14972	14991	TTAGAAAAAGAATGAAAGAC	27	1495
1101941	N/A	N/A	14991	15010	CTGGATACAACTCACAGTGT	63	1496
1101943	N/A	N/A	15141	15160	TGCAGTAGCCATTACCTGTT	87	1497
1101945	N/A	N/A	15217	15236	AACAGGCACCAAGAGCAGCA	82	1498
1101946	N/A	N/A	15292	15311	GGTAGCCAACAAAGAAGCAA	64	1499
1101947	N/A	N/A	15295	15314	CAAGGTAGCCAACAAAGAAG	85	1500
1101948	N/A	N/A	15297	15316	TCCAAGGTAGCCAACAAAGA	72	1501
1101949	N/A	N/A	15318	15337	CTGAAAATTCACTATCTGCC	67	1502
1101950	N/A	N/A	15321	15340	TTTCTGAAAATTCACTATCT	79	1503
1101951	N/A	N/A	15324	15343	AAATTTCTGAAAATTCACTA	76	1504
1101952	N/A	N/A	15367	15386	AAATGCAAACCTGTTTATTT	68	1505
1101953	N/A	N/A	15441	15460	CTGGGCATTTAAACTGAAGG	72	1506
1101954	N/A	N/A	15461	15480	TCTACCAAAATAAGTTCTCC	99	1507
1101955	N/A	N/A	15465	15484	CATATCTACCAAAATAAGTT	76	1508
1101956	N/A	N/A	15503	15522	AAAATTATATTCAACTTGCT	93	1509
1101957	N/A	N/A	15519	15538	TGGGTGCTACTTTAGAAAAA	58	1510
1101958	N/A	N/A	15552	15571	GTCTACTATATACATCTGAT	48	1511
1101959	N/A	N/A	15555	15574	CTAGTCTACTATATACATCT	59	1512
1101960	N/A	N/A	15556	15575	ACTAGTCTACTATATACATC	77	1513
1101961	N/A	N/A	15561	15580	TTAAAACTAGTCTACTATAT	85	1514
1101962	N/A	N/A	15585	15604	ATATTCTACCCATAAGTGCT	34	1515
1101963	N/A	N/A	15588	15607	TGTATATTCTACCCATAAGT	66	1516
1101964	N/A	N/A	15601	15620	TCAAAAATCCAGATGTATAT	98	1517
1101965	N/A	N/A	15603	15622	CCTCAAAAATCCAGATGTAT	82	1518
1101966	N/A	N/A	15604	15623	GCCTCAAAAATCCAGATGTA	98	1519
1101967	N/A	N/A	15624	15643	CACAATTCCTAAATAAAACT	106	1520
1101968	N/A	N/A	15626	15645	CACACAATTCCTAAATAAAA	89	1521
1101969	N/A	N/A	15635	15654	CCAGAAAACCACACAATTCC	87	1522

1101970	N/A	N/A	15636	15655	TCCAGAAAACCACACAATTC	83	1523
1101971	N/A	N/A	15637	15656	TTCCAGAAAACCACACAATT	79	1524
1101972	N/A	N/A	15640	15659	ATGTTCCAGAAAACCACACA	66	1525
1101973	N/A	N/A	15643	15662	GAGATGTTCCAGAAAACCAC	43	1526
1101974	N/A	N/A	15666	15685	AGTGCTTTTCATACCAGGTC	6	1527
1101975	N/A	N/A	15667	15686	GAGTGCTTTTCATACCAGGT	6	1528
1101976	N/A	N/A	15704	15723	CACTAAATCCATAAAAAAAA	110	1529
1101977	N/A	N/A	15706	15725	ATCACTAAATCCATAAAAAA	101	1530
1101979	N/A	N/A	15712	15731	AGATATATCACTAAATCCAT	51	1531
1101981	N/A	N/A	15714	15733	ATAGATATATCACTAAATCC	63	1532
1101982	N/A	N/A	15715	15734	TATAGATATATCACTAAATC	103	1533
1101983	N/A	N/A	15719	15738	TGTGTATAGATATATCACTA	76	1534
1101984	N/A	N/A	15720	15739	GTGTGTATAGATATATCACT	54	1535
1101985	N/A	N/A	15739	15758	TATAGGTTTTAAAAAGTGTG	42	1536
1101986	N/A	N/A	16063	16082	TATAAATTTCTCTAGAAGGC	58	1537
1101987	N/A	N/A	16064	16083	ATATAAATTTCTCTAGAAGG	78	1538
1101988	N/A	N/A	16068	16087	TCATATATAAATTTCTCTAG	102	1539
1101989	N/A	N/A	16110	16129	CCATTCCAAATTTAGGAAGT	74	1540
1101990	N/A	N/A	16113	16132	ACTCCATTCCAAATTTAGGA	60	1541
1101991	N/A	N/A	16136	16155	AGCAACTTTTCATAAGCTAA	75	1542
1101992	N/A	N/A	16160	16179	TGCTTATAACCTGTTAAGAA	28	1543
1101993	N/A	N/A	16258	16277	GAAATGCAAAACAGAATCTT	70	1544
1101994	N/A	N/A	16297	16316	TTACAACTTTAAAAATCAAA	72	1545
1101995	N/A	N/A	16306	16325	TTTAAGAAATTACAACTTTA	89	1546
1101996	N/A	N/A	16330	16349	AGTATTCAAAATGTATTTCT	80	1547
1101997	N/A	N/A	16345	16364	GAACATCAAAACAAAAGTAT	86	1548
1101998	N/A	N/A	16385	16404	CACAAAGGTGAAATAGGAAA	66	1549
1101999	N/A	N/A	16529	16548	ATCACACAACCATATGAACG	70	1550
1102000	N/A	N/A	16538	16557	TTTTAAAAGATCACACAACC	86	1551
1102001	N/A	N/A	16540	16559	GTTTTTAAAAGATCACACAA	60	1552
1102002	N/A	N/A	16543	16562	GATGTTTTTAAAAGATCACA	61	1553
1102003	N/A	N/A	16546	16565	ACTGATGTTTTTAAAAGATC	45	1554
1102004	N/A	N/A	16547	16566	CACTGATGTTTTTAAAAGAT	53	1555
1102005	N/A	N/A	16571	16590	AAGATTATATTTATAGTTAA	121	1556
1102006	N/A	N/A	16572	16591	TAAGATTATATTTATAGTTA	94	1557
1102007	N/A	N/A	16581	16600	GTGATAATTTAAGATTATAT	51	1558
1102008	N/A	N/A	16584	16603	TTTGTGATAATTTAAGATTA	125	1559
1102009	N/A	N/A	16588	16607	AAAATTTGTGATAATTTAAG	136	1560
1102010	N/A	N/A	16601	16620	GCAAATATTATATAAAATTT	85	1561
1102011	N/A	N/A	16603	16622	TGGCAAATATTATATAAAAT	84	1562
1102012	N/A	N/A	16627	16646	TGAATTCATATTTATGTTGT	54	1563
1102013	N/A	N/A	16637	16656	CTTGAAATATTGAATTCATA	85	1564
1102015	N/A	N/A	16655	16674	GAAAACAGACAATATTAACT	89	1565

1102017	N/A	N/A	16680	16699	TAAATGATCTTTCATTTCTA	57	1566
1102018	N/A	N/A	16732	16751	ACCTGTTTTCCTAATTTTCT	68	1567
1102019	N/A	N/A	16748	16767	AAGGGTAAGAAATGTTACCT	113	1568
1102020	N/A	N/A	16768	16787	TATAAGAAAAAAAGACAAGG	114	1569
1102021	N/A	N/A	16771	16790	CAATATAAGAAAAAAAGACA	85	1570
1102022	N/A	N/A	16800	16819	TGGCCCACATTTTAGTTTTA	91	1571
1102023	N/A	N/A	17168	17187	AATTTTAAAGTCAGCAATCC	43	1572
1102024	N/A	N/A	17172	17191	TCCTAATTTTAAAGTCAGCA	8	1573
1102025	N/A	N/A	17173	17192	TTCCTAATTTTAAAGTCAGC	102	1574
1102026	N/A	N/A	17174	17193	TTTCCTAATTTTAAAGTCAG	88	1575
1102027	N/A	N/A	17175	17194	GTTTCCTAATTTTAAAGTCA	26	1576
1102028	N/A	N/A	17180	17199	GGTCAGTTTCCTAATTTTAA	4	1577
1102029	N/A	N/A	17237	17256	AATGACAATTTCTATCTATC	64	1578
1102030	N/A	N/A	17252	17271	GATATTATCTTTTAAAATGA	88	1579
1102031	N/A	N/A	17277	17296	CACAAATAAATTTATAAGGA	108	1580
1102032	N/A	N/A	17283	17302	ACTTGTCACAAATAAATTTA	113	1581
1102033	N/A	N/A	17284	17303	TACTTGTCACAAATAAATTT	77	1582
1102034	N/A	N/A	17300	17319	ATAGTTAAATTGCATATACT	57	1583
1102035	N/A	N/A	17304	17323	TGATATAGTTAAATTGCATA	51	1584
1102036	N/A	N/A	17312	17331	TTTTCTTATGATATAGTTAA	70	1585
1102037	N/A	N/A	17318	17337	TAGAATTTTTCTTATGATAT	78	1586
1102038	N/A	N/A	17319	17338	ATAGAATTTTTCTTATGATA	83	1587
1102039	N/A	N/A	17323	17342	TAATATAGAATTTTTCTTAT	94	1588
1102040	N/A	N/A	17335	17354	TTGTATTATCTTTAATATAG	66	1589
1102041	N/A	N/A	17365	17384	ACATAAAAACCCACTTAAAA	89	1590
1102042	N/A	N/A	17369	17388	CATCACATAAAAACCCACTT	59	1591
1102043	N/A	N/A	17378	17397	GAACATAGTCATCACATAAA	25	1592
1102044	N/A	N/A	17380	17399	CAGAACATAGTCATCACATA	47	1593
1102045	N/A	N/A	17417	17436	TGCTAAATACAAATCTATAA	97	1594
1102046	N/A	N/A	17419	17438	TATGCTAAATACAAATCTAT	116	1595
1102047	N/A	N/A	17420	17439	CTATGCTAAATACAAATCTA	94	1596
1102048	N/A	N/A	17421	17440	ACTATGCTAAATACAAATCT	70	1597
1102049	N/A	N/A	17446	17465	ACACTATTTCAGGCTTTGTG	15	1598
1102051	N/A	N/A	17464	17483	ATGCTTTATTCATGCTTGAC	29	1599
1102053	N/A	N/A	17494	17513	ATAATCTTACACTAAAGCAA	85	1600
1102054	N/A	N/A	17497	17516	TGAATAATCTTACACTAAAG	86	1601
1102055	N/A	N/A	17498	17517	ATGAATAATCTTACACTAAA	81	1602
1102056	N/A	N/A	17505	17524	AATCATAATGAATAATCTTA	85	1603
1102057	N/A	N/A	17576	17595	AGACATATTTCATGTTTTAT	40	1604
1102058	N/A	N/A	17577	17596	AAGACATATTTCATGTTTTA	64	1605
1102059	N/A	N/A	17578	17597	CAAGACATATTTCATGTTTT	56	1606
1102060	N/A	N/A	17583	17602	TTGCTCAAGACATATTTCAT	30	1607
1102061	N/A	N/A	17584	17603	CTTGCTCAAGACATATTTCA	84	1608

1102062	N/A	N/A	17599	17618	TGTTTCTTAAAATAGCTTGC	33	1609
1102063	N/A	N/A	17632	17651	TTCAAAATTCTAATAACAAG	104	1610
1102064	N/A	N/A	17635	17654	AGATTCAAAATTCTAATAAC	121	1611
1102065	N/A	N/A	17644	17663	CTCTTTCAAAGATTCAAAAT	72	1612
1102066	N/A	N/A	17647	17666	ACCCTCTTTCAAAGATTCAA	64	1613
1102067	N/A	N/A	17654	17673	TTCAATAACCCTCTTTCAAA	89	1614
1102068	N/A	N/A	17779	17798	TAAATGATACCATACAGCAG	69	1615
1102069	N/A	N/A	17783	17802	TTAATAAATGATACCATACA	79	1616
1102070	N/A	N/A	17794	17813	TTTCTAGACTTTTAATAAAT	91	1617
1102071	N/A	N/A	17941	17960	TACTACAACCAAGATAGTGA	93	1618
1102072	N/A	N/A	17963	17982	TACTGTACTCCCATGAAACC	61	1619
1102073	N/A	N/A	17971	17990	CATTTGTATACTGTACTCCC	28	1620
1102074	N/A	N/A	18368	18387	TTGGCTTGTATTTACATTTT	6	1621
1102075	N/A	N/A	18406	18425	AGATTTAATTCAATATATTT	79	1622
1102076	N/A	N/A	18413	18432	CTCTTACAGATTTAATTCAA	49	1623
1102077	N/A	N/A	18427	18446	TGTTTTTGAATTATCTCTTA	19	1624
1102078	N/A	N/A	18448	18467	AAAAGATAACAATAGGGTTT	53	1625
1102079	N/A	N/A	18449	18468	TAAAAGATAACAATAGGGTT	57	1626
1102080	N/A	N/A	18452	18471	ACTTAAAAGATAACAATAGG	85	1627
1102081	N/A	N/A	18454	18473	TGACTTAAAAGATAACAATA	88	1628
1102082	N/A	N/A	18458	18477	TGGGTGACTTAAAAGATAAC	81	1629
1102083	N/A	N/A	18461	18480	ATTTGGGTGACTTAAAAGAT	83	1630
1102084	N/A	N/A	18478	18497	GACTTTTCCCAAATTTGATT	11	1631
1102085	N/A	N/A	18480	18499	GTGACTTTTCCCAAATTTGA	18	1632
1102087	N/A	N/A	18833	18852	TTAAGAAAGAACCAACTTAG	92	1633
1102089	N/A	N/A	18844	18863	CAGGAAGAACTTTAAGAAAG	52	1634
1102090	N/A	N/A	18875	18894	GTTACATCTCCTTAACTTGC	14	1635
1102091	N/A	N/A	18903	18922	CCAGCTAGCCTCCACTGTAA	76	1636
1102092	N/A	N/A	18905	18924	ACCCAGCTAGCCTCCACTGT	168	1637
1102093	N/A	N/A	19119	19138	TTAAATAATCTCAGCAGTAC	43	1638
1102094	N/A	N/A	19123	19142	GAGGTTAAATAATCTCAGCA	82	1639
1102095	N/A	N/A	19124	19143	AGAGGTTAAATAATCTCAGC	67	1640
1102096	N/A	N/A	19125	19144	CAGAGGTTAAATAATCTCAG	95	1641
1102097	N/A	N/A	19126	19145	CCAGAGGTTAAATAATCTCA	98	1642
1102098	N/A	N/A	19127	19146	CCCAGAGGTTAAATAATCTC	69	1643
1102099	N/A	N/A	19135	19154	AAATAAAACCCAGAGGTTAA	79	1644
1102100	N/A	N/A	19136	19155	TAAATAAAACCCAGAGGTTA	81	1645
1102101	N/A	N/A	19137	19156	ATAAATAAAACCCAGAGGTT	85	1646
1102102	N/A	N/A	19192	19211	GCTTACTTTATACAAAAAAA	65	1647
1102103	N/A	N/A	19194	19213	GTGCTTACTTTATACAAAAA	17	1648
1102104	N/A	N/A	19196	19215	CAGTGCTTACTTTATACAAA	4	1649
1102105	N/A	N/A	19207	19226	CCTTAAAAATTCAGTGCTTA	31	1650
1102106	N/A	N/A	19208	19227	ACCTTAAAAATTCAGTGCTT	29	1651

1102107	N/A	N/A	19216	19235	TTAATACAACCTTAAAAATT	87	1652
1102108	N/A	N/A	19222	19241	TGCAAATTAATACAACCTTA	17	1653
1102109	N/A	N/A	19232	19251	GACATTTATTTGCAAATTAA	30	1654
1102110	N/A	N/A	19238	19257	AAGATAGACATTTATTTGCA	12	1655
1102111	N/A	N/A	19239	19258	TAAGATAGACATTTATTTGC	27	1656
1102112	N/A	N/A	19241	19260	AATAAGATAGACATTTATTT	112	1657
1102113	N/A	N/A	19246	19265	AAAATAATAAGATAGACATT	100	1658
1102114	N/A	N/A	19249	19268	CTCAAAATAATAAGATAGAC	108	1659
1102115	N/A	N/A	19250	19269	TCTCAAAATAATAAGATAGA	71	1660
1102116	N/A	N/A	19251	19270	CTCTCAAAATAATAAGATAG	100	1661
1102117	N/A	N/A	19265	19284	AAAATTTTTTAAATCTCTCA	97	1662
1102118	N/A	N/A	19296	19315	TCAAAATGTGAAAATGCAAT	81	1663
1102119	N/A	N/A	19340	19359	AACCAAAATTTGACATCTTC	23	1664
1102120	N/A	N/A	19343	19362	ATAAACCAAAATTTGACATC	75	1665
1102121	N/A	N/A	19346	19365	AAAATAAACCAAAATTTGAC	126	1666
1102123	N/A	N/A	19393	19412	ATAGTGAAAAATATAGTTTT	91	1667
1102125	N/A	N/A	19395	19414	CTATAGTGAAAAATATAGTT	92	1668
1102126	N/A	N/A	19397	19416	GTCTATAGTGAAAAATATAG	90	1669
1102127	N/A	N/A	19430	19449	TTCATTATACAGGGACCTCG	60	1670
1102128	N/A	N/A	19437	19456	CTTCTTTTTCATTATACAGG	11	1671
1102129	N/A	N/A	19453	19472	TAATACTTTTTCCAGCCTTC	17	1672
1102130	N/A	N/A	19455	19474	GTTAATACTTTTTCCAGCCT	9	1673
1102131	N/A	N/A	19457	19476	ATGTTAATACTTTTTCCAGC	10	1674
1102132	N/A	N/A	19458	19477	AATGTTAATACTTTTTCCAG	63	1675
1102133	N/A	N/A	19460	19479	ACAATGTTAATACTTTTTCC	108	1676
1102134	N/A	N/A	19468	19487	GGATTTTGACAATGTTAATA	20	1677
1102135	N/A	N/A	19498	19517	CGATCAATATCATGACCAAC	46	1678
1102136	N/A	N/A	19517	19536	AAAAAGTTTCTAAAGTTAAC	187	1679
1102137	N/A	N/A	19527	19546	CACAAGATACAAAAAGTTTC	107	1680
1102138	N/A	N/A	19530	19549	ACCCACAAGATACAAAAAGT	87	1681
1102139	N/A	N/A	19531	19550	AACCCACAAGATACAAAAAG	101	1682
1102140	N/A	N/A	19532	19551	TAACCCACAAGATACAAAAA	88	1683
1102141	N/A	N/A	19537	19556	TAATTTAACCCACAAGATAC	65	1684
1102142	N/A	N/A	19538	19557	CTAATTTAACCCACAAGATA	75	1685
1102143	N/A	N/A	19542	19561	AATCCTAATTTAACCCACAA	58	1686
1102144	N/A	N/A	19544	19563	GTAATCCTAATTTAACCCAC	39	1687
1102145	N/A	N/A	19548	19567	CATAGTAATCCTAATTTAAC	94	1688
1102146	N/A	N/A	19564	19583	TCATTTATCACTACCACATA	64	1689
1102147	N/A	N/A	19567	19586	ACATCATTTATCACTACCAC	27	1690
1102148	N/A	N/A	19571	19590	ATTAACATCATTTATCACTA	80	1691
1102149	N/A	N/A	19574	19593	CTAATTAACATCATTTATCA	109	1692
1102150	N/A	N/A	19575	19594	CCTAATTAACATCATTTATC	88	1693
1102151	N/A	N/A	19576	19595	CCCTAATTAACATCATTTAT	91	1694

1102152	N/A	N/A	19577	19596	GCCCTAATTAACATCATTTA	88	1695
1102153	N/A	N/A	19579	19598	CGGCCCTAATTAACATCATT	118	1696
1102154	N/A	N/A	19580	19599	TCGGCCCTAATTAACATCAT	76	1697
1102155	N/A	N/A	19581	19600	CTCGGCCCTAATTAACATCA	88	1698
1102156	N/A	N/A	19585	19604	TGCACTCGGCCCTAATTAAC	55	1699
1102157	N/A	N/A	19685	19704	GGTCTTACACTATGTTGTAC	73	1700
1102159	N/A	N/A	19881	19900	CACATATAACATATAAACAC	99	1701
1102161	N/A	N/A	19883	19902	ATCACATATAACATATAAAC	108	1702
1102162	N/A	N/A	19887	19906	CACTATCACATATAACATAT	45	1703
1102163	N/A	N/A	19918	19937	GTCTCTATAATTTAAAAATG	95	1704
1102164	N/A	N/A	20063	20082	CAGCTCAGTTTTTAAAAATC	55	1705
1102165	N/A	N/A	20074	20093	TTTATAATTACCAGCTCAGT	36	1706
1102166	N/A	N/A	20077	20096	GAATTTATAATTACCAGCTC	23	1707
1102167	N/A	N/A	20084	20103	AGGAAGAGAATTTATAATTA	98	1708
1102168	N/A	N/A	20105	20124	TGTGAGAAAGTCAGAAGTTC	61	1709
1102169	N/A	N/A	20122	20141	TGTCAAAAGATTCCAATTGT	118	1710
1102170	N/A	N/A	20124	20143	TTTGTCAAAAGATTCCAATT	77	1711
1102171	N/A	N/A	20128	20147	AATTTTTGTCAAAAGATTCC	68	1712
1102172	N/A	N/A	20147	20166	AAGTTTTCCCATTACTGATA	49	1713
1102173	N/A	N/A	20163	20182	AAATGACAACTACACAAAGT	96	1714
1102174	N/A	N/A	20204	20223	CAACATAACTCCAATCATAT	97	1715
1102175	N/A	N/A	20222	20241	TTTTTCAAAATATCAGTCCA	45	1716
1102176	N/A	N/A	20223	20242	TTTTTTCAAAATATCAGTCC	55	1717
1102177	N/A	N/A	20238	20257	AGCTATAATTAAATCTTTTT	67	1718
1102178	N/A	N/A	20253	20272	AATGTCTTTATTAATAGCTA	47	1719
1102179	N/A	N/A	20254	20273	AAATGTCTTTATTAATAGCT	70	1720
1102180	N/A	N/A	20264	20283	TCAGTAGTTTAAATGTCTTT	18	1721
1102181	N/A	N/A	20289	20308	CTCCCAAAAGAATAAAAATG	97	1722
1102182	N/A	N/A	20294	20313	AAACCCTCCCAAAAGAATAA	92	1723
1102183	N/A	N/A	20299	20318	ACATTAAACCCTCCCAAAAG	83	1724
1102184	N/A	N/A	20300	20319	AACATTAAACCCTCCCAAAA	90	1725
1102185	N/A	N/A	20304	20323	TATAAACATTAAACCCTCCC	102	1726
1102186	N/A	N/A	20306	20325	ACTATAAACATTAAACCCTC	117	1727
1102187	N/A	N/A	20307	20326	AACTATAAACATTAAACCCT	86	1728
1102188	N/A	N/A	20311	20330	TTTAAACTATAAACATTAAA	87	1729
1102189	N/A	N/A	20314	20333	TGCTTTAAACTATAAACATT	72	1730
1102190	N/A	N/A	20315	20334	TTGCTTTAAACTATAAACAT	84	1731
1102191	N/A	N/A	20316	20335	TTTGCTTTAAACTATAAACA	91	1732
1102192	N/A	N/A	20318	20337	AGTTTGCTTTAAACTATAAA	75	1733
1102193	N/A	N/A	20976	20995	TATCACTATTAAATACTTTT	70	1734
1102195	N/A	N/A	20988	21007	ATACTGCAGATTTATCACTA	26	1735
1102197	N/A	N/A	21022	21041	GACTGAATAATATGATCTTA	27	1736
1102198	N/A	N/A	21051	21070	GAAATATTTCAAGTTGAGCT	15	1737

1102199	N/A	N/A	21053	21072	TGGAAATATTTCAAGTTGAG	27	1738
1102200	N/A	N/A	21054	21073	CTGGAAATATTTCAAGTTGA	15	1739
1102201	N/A	N/A	21055	21074	TCTGGAAATATTTCAAGTTG	43	1740
1102202	N/A	N/A	21069	21088	AAGATTGTTTAAACTCTGGA	16	1741
1102203	N/A	N/A	21093	21112	AGATACAACCCATCAAAGCT	89	1742
1102204	N/A	N/A	21094	21113	TAGATACAACCCATCAAAGC	145	1743
1102205	N/A	N/A	21101	21120	TTAAGAATAGATACAACCCA	99	1744
1102206	N/A	N/A	21106	21125	ACATGTTAAGAATAGATACA	86	1745
1102207	N/A	N/A	21116	21135	AGGAAGTTTCACATGTTAAG	71	1746
1102208	N/A	N/A	21152	21171	TGTCAATATTTAAGTTAGTG	93	1747
1102209	N/A	N/A	21153	21172	TTGTCAATATTTAAGTTAGT	77	1748
1102210	N/A	N/A	21154	21173	ATTGTCAATATTTAAGTTAG	84	1749
1102211	N/A	N/A	21178	21197	TTCAAGTTAAACCACTGGAA	77	1750
1102212	N/A	N/A	21180	21199	AATTCAAGTTAAACCACTGG	67	1751
1102213	N/A	N/A	21260	21279	TTACTTACCTTCCTGTTGTA	73	1752
1102214	N/A	N/A	21284	21303	GTAACATTACAAAATGTTCA	78	1753
1102215	N/A	N/A	21304	21323	TTATTTAACTACTTCGAAAG	84	1754
1102216	N/A	N/A	21311	21330	TGCCTGGTTATTTAACTACT	27	1755
1102217	N/A	N/A	21398	21417	CAAATCACAGCCTATCACCA	93	1756
1102218	N/A	N/A	21402	21421	CACCCAAATCACAGCCTATC	82	1757
1102219	N/A	N/A	21403	21422	TCACCCAAATCACAGCCTAT	62	1758
1102220	N/A	N/A	21404	21423	GTCACCCAAATCACAGCCTA	46	1759
1102221	N/A	N/A	21495	21514	AGAAAAAGCCATTACTTAGA	51	1760
1102222	N/A	N/A	21497	21516	AAAGAAAAAGCCATTACTTA	89	1761
1102223	N/A	N/A	21604	21623	CATGTATTTCAAAGAAACTG	62	1762
1102224	N/A	N/A	21955	21974	CAAGGGATAGTTTAATCTAG	70	1763
1102225	N/A	N/A	22004	22023	GATCCTAAAATCACTGATGA	85	1764
1102226	N/A	N/A	22005	22024	AGATCCTAAAATCACTGATG	64	1765
1102227	N/A	N/A	22007	22026	TCAGATCCTAAAATCACTGA	83	1766
1102228	N/A	N/A	22008	22027	GTCAGATCCTAAAATCACTG	47	1767
1102229	N/A	N/A	22009	22028	AGTCAGATCCTAAAATCACT	64	1768
1102231	N/A	N/A	22067	22086	GACGATACAGAAATAATTAA	73	1769
1102233	N/A	N/A	22204	22223	AACATGGTTTAAAGATAGGA	85	1770
1102234	N/A	N/A	22213	22232	AACAGACAAAACATGGTTTA	75	1771
1102235	N/A	N/A	22240	22259	GGGTTTAAAGAATGGCTGGA	64	1772
1102236	N/A	N/A	22244	22263	AGTAGGGTTTAAAGAATGGC	65	1773
1102237	N/A	N/A	22330	22349	CAATGGAGTGATTATGATGA	63	1774
1102238	N/A	N/A	22381	22400	TTTGTCATTCAAGTATGATG	41	1775
1102239	N/A	N/A	22403	22422	TGGTTTAACCAGGGTTGAGA	18	1776
1102240	N/A	N/A	22462	22481	TATGTTATTTTTTAGCCACG	61	1777
1102241	N/A	N/A	22464	22483	TTTATGTTATTTTTTAGCCA	89	1778
1102242	N/A	N/A	22480	22499	AAACCAATCATCATGTTTTA	55	1779
1102243	N/A	N/A	22481	22500	AAAACCAATCATCATGTTTT	56	1780

1102244	N/A	N/A	22482	22501	TAAAACCAATCATCATGTTT	47	1781
1102245	N/A	N/A	22486	22505	AAAGTAAAACCAATCATCAT	84	1782
1102246	N/A	N/A	22505	22524	GGATAGATCATTTAAGAAAA	38	1783
1102247	N/A	N/A	22589	22608	ATGAGCTGTGATTATGCTGC	82	1784
1102248	N/A	N/A	22691	22710	AAAGTAAAACCTTAGCTAGG	74	1785
1102249	N/A	N/A	22692	22711	TAAAGTAAAACCTTAGCTAG	105	1786
1102250	N/A	N/A	22695	22714	ATTTAAAGTAAAACCTTAGC	110	1787
1102251	N/A	N/A	22701	22720	TAATAAATTTAAAGTAAAAC	111	1788
1102252	N/A	N/A	22706	22725	GATTATAATAAATTTAAAGT	76	1789
1102253	N/A	N/A	22710	22729	TTGTGATTATAATAAATTTA	77	1790
1102254	N/A	N/A	22711	22730	TTTGTGATTATAATAAATTT	109	1791
1102255	N/A	N/A	22713	22732	ATTTTGTGATTATAATAAAT	97	1792
1102256	N/A	N/A	22715	22734	GAATTTTGTGATTATAATAA	112	1793
1102257	N/A	N/A	22748	22767	GTAGAAATATCAGACAGCAC	82	1794
1102258	N/A	N/A	22752	22771	CATAGTAGAAATATCAGACA	108	1795
1102259	N/A	N/A	22754	22773	AACATAGTAGAAATATCAGA	86	1796
1102260	N/A	N/A	22762	22781	ACTAAGAAAACATAGTAGAA	81	1797
1102261	N/A	N/A	22794	22813	TTTTTTATAAACACCTTGGA	73	1798
1102262	N/A	N/A	22860	22879	GTGAAATTAGTCACCTTGGA	18	1799
1102263	N/A	N/A	22865	22884	AAGCTGTGAAATTAGTCACC	41	1800
1102264	N/A	N/A	22867	22886	ATAAGCTGTGAAATTAGTCA	58	1801
1102265	N/A	N/A	22883	22902	TTAAAGGTTTAAAGACATAA	109	1802
1102267	N/A	N/A	22965	22984	AACATAATTTTAATTGCTTC	62	1803
1102269	N/A	N/A	22967	22986	AGAACATAATTTTAATTGCT	75	1804
1102270	N/A	N/A	22997	23016	ATAAGCAAATTGATAAATTT	91	1805
1102271	N/A	N/A	23008	23027	CAGGTGAAGATATAAGCAAA	66	1806
1102272	N/A	N/A	23010	23029	CACAGGTGAAGATATAAGCA	78	1807
1102273	N/A	N/A	23012	23031	AGCACAGGTGAAGATATAAG	68	1808
1102274	N/A	N/A	23037	23056	CATTCATCTATTTAAATAGG	64	1809
1102275	N/A	N/A	23150	23169	GAACTGATTATATAAGAGAG	74	1810
1102276	N/A	N/A	23175	23194	GGAATATTACAAAAAAAGGG	102	1811
1102277	N/A	N/A	23289	23308	AGAGACAATCCTAAGGAAAA	93	1812
1102278	N/A	N/A	23290	23309	TAGAGACAATCCTAAGGAAA	52	1813
1102279	N/A	N/A	23293	23312	CACTAGAGACAATCCTAAGG	69	1814
1102280	N/A	N/A	23603	23622	ATGGAGAAACCCCTTCCATC	74	1815
1102281	N/A	N/A	23874	23893	ATACCATTACTAAAAGATGG	79	1816
1102282	N/A	N/A	23879	23898	TCCAAATACCATTACTAAAA	49	1817
1102283	N/A	N/A	23880	23899	CTCCAAATACCATTACTAAA	41	1818
1102284	N/A	N/A	23883	23902	GATCTCCAAATACCATTACT	42	1819
1102285	N/A	N/A	23900	23919	GCCAGCACTCAAATTGTGAT	53	1820
1102286	N/A	N/A	23927	23946	CATAACAAACCCAGCAGCAA	91	1821
1102287	N/A	N/A	23933	23952	TAACTACATAACAAACCCAG	85	1822
1102288	N/A	N/A	23936	23955	CAATAACTACATAACAAACC	81	1823

1102289	N/A	N/A	23937	23956	ACAATAACTACATAACAAAC	96	1824
1102290	N/A	N/A	23939	23958	TCACAATAACTACATAACAA	74	1825
1102291	N/A	N/A	23940	23959	TTCACAATAACTACATAACA	78	1826
1102292	N/A	N/A	23941	23960	ATTCACAATAACTACATAAC	85	1827
1102293	N/A	N/A	23945	23964	GTGAATTCACAATAACTACA	61	1828
1102294	N/A	N/A	23946	23965	TGTGAATTCACAATAACTAC	88	1829
1102295	N/A	N/A	23947	23966	ATGTGAATTCACAATAACTA	89	1830
1102296	N/A	N/A	23959	23978	CTATATTCCTAAATGTGAAT	85	1831
1102297	N/A	N/A	23964	23983	AAACCCTATATTCCTAAATG	107	1832
1102298	N/A	N/A	23970	23989	AATTAAAAAACCCTATATTCC	91	1833
1102299	N/A	N/A	23971	23990	GAATTAAAAAACCCTATATTC	93	1834
1102300	N/A	N/A	23984	24003	ATCTAAAATCAAAGAATTAA	93	1835
1102301	N/A	N/A	23985	24004	TATCTAAAATCAAAGAATTA	127	1836
1102303	N/A	N/A	23987	24006	AGTATCTAAAATCAAAGAAT	93	1837
1102305	N/A	N/A	23990	24009	ACAAGTATCTAAAATCAAAG	83	1838
1102306	N/A	N/A	23991	24010	TACAAGTATCTAAAATCAAA	124	1839
1102307	N/A	N/A	23998	24017	AAAAAGATACAAGTATCTAA	113	1840
1102308	N/A	N/A	24001	24020	AGAAAAAAGATACAAGTATC	82	1841
1102309	N/A	N/A	24017	24036	AGGTTTTAAATATAAAAGAA	94	1842
1102310	N/A	N/A	24020	24039	CCAAGGTTTTAAATATAAAA	75	1843
1102311	N/A	N/A	24070	24089	GCTGAAGGCCAAAGGTAGAC	72	1844
1102312	N/A	N/A	24092	24111	TAGGAAAACCACAGCATGGT	85	1845
1102313	N/A	N/A	24093	24112	TTAGGAAAACCACAGCATGG	80	1846
1102314	N/A	N/A	24094	24113	GTTAGGAAAACCACAGCATG	94	1847
1102315	N/A	N/A	24145	24164	ACAGATGATATTTAAGATCC	66	1848
1102316	N/A	N/A	24158	24177	ATAGATCTTATTTACAGATG	103	1849
1102317	N/A	N/A	24194	24213	CAAGACTAAAGATAAAAGTT	85	1850
1102318	N/A	N/A	24197	24216	TGTCAAGACTAAAGATAAAA	82	1851
1102319	N/A	N/A	24199	24218	GATGTCAAGACTAAAGATAA	76	1852
1102320	N/A	N/A	24229	24248	GGAGTTAGTCAAAGCTAGGT	47	1853
1102321	N/A	N/A	24231	24250	TAGGAGTTAGTCAAAGCTAG	62	1854
1102322	N/A	N/A	24246	24265	TGGAGATGCCAAAGCTAGGA	28	1855
1102323	N/A	N/A	24292	24311	TCTTTCATAGACATGTTCAG	64	1856
1102324	N/A	N/A	24297	24316	ATAAGTCTTTCATAGACATG	98	1857
1102325	N/A	N/A	24337	24356	AATGGAAAACCTGATGGATA	84	1858
1102326	N/A	N/A	24355	24374	AAGAGTCACCCTTATGGAAA	68	1859
1102327	N/A	N/A	24382	24401	CGGTATAATATATAGGAACC	48	1860
1102328	N/A	N/A	24384	24403	GTCGGTATAATATATAGGAA	23	1861
1102329	N/A	N/A	24819	24838	GGTTTTATTCAAGACTTCAC	9	1862
1102330	N/A	N/A	24823	24842	CTTGGGTTTTATTCAAGACT	54	1863
1102331	N/A	N/A	24892	24911	ACCATGGTATTCTATGAAGA	70	1864
1102332	N/A	N/A	24909	24928	AATAAATATGCCAGCTCACC	39	1865
1102333	N/A	N/A	24914	24933	TGTATAATAAATATGCCAGC	23	1866

1102334	N/A	N/A	24915	24934	TTGTATAATAAATATGCCAG	31	1867
1102335	N/A	N/A	24936	24955	GCCAGTAAAATTGTTTCTGT	41	1868
1102336	N/A	N/A	24994	25013	TGAACATTTTTTATGAGGAC	8	1869
1102337	N/A	N/A	24995	25014	TTGAACATTTTTTATGAGGA	26	1870
1102339	N/A	N/A	25019	25038	AATGGAAAACCTCAAAATAG	75	1871
1102341	N/A	N/A	25438	25457	ATCTAACTGATTTAAGTTTC	112	1872
1102342	N/A	N/A	25449	25468	TACCTAAAACAATCTAACTG	103	1873
1102343	N/A	N/A	25453	25472	GCTATACCTAAAACAATCTA	68	1874
1102344	N/A	N/A	25454	25473	GGCTATACCTAAAACAATCT	55	1875
1102345	N/A	N/A	25455	25474	GGGCTATACCTAAAACAATC	55	1876
1102346	N/A	N/A	25457	25476	ATGGGCTATACCTAAAACAA	101	1877
1102347	N/A	N/A	25473	25492	CACACAAAAACCAAGGATGG	59	1878
1102348	N/A	N/A	25499	25518	CCAGGGTTTCCCCAAGCTAG	54	1879
1102349	N/A	N/A	25507	25526	CCAGAAATCCAGGGTTTCCC	73	1880
1102350	N/A	N/A	25509	25528	TTCCAGAAATCCAGGGTTTC	56	1881
1102351	N/A	N/A	25513	25532	ATGATTCCAGAAATCCAGGG	18	1882
1102352	N/A	N/A	25515	25534	ATATGATTCCAGAAATCCAG	41	1883
1102353	N/A	N/A	25521	25540	GTCTAAATATGATTCCAGAA	6	1884
1102354	N/A	N/A	25545	25564	ATTACATTAGTCTAGTGTGA	51	1885
1102355	N/A	N/A	25550	25569	AAAGAATTACATTAGTCTAG	64	1886
1102356	N/A	N/A	25551	25570	AAAAGAATTACATTAGTCTA	87	1887
1102357	N/A	N/A	25554	25573	CCCAAAAGAATTACATTAGT	60	1888
1102358	N/A	N/A	25555	25574	TCCCAAAAGAATTACATTAG	67	1889
1102359	N/A	N/A	25556	25575	ATCCCAAAAGAATTACATTA	95	1890
1102360	N/A	N/A	25561	25580	TTTGCATCCCAAAAGAATTA	75	1891
1102361	N/A	N/A	25590	25609	AAAAGCTATTTAAGGTGTCA	26	1892
1102362	N/A	N/A	25591	25610	TAAAAGCTATTTAAGGTGTC	56	1893
1102363	N/A	N/A	25592	25611	CTAAAAGCTATTTAAGGTGT	67	1894
1102364	N/A	N/A	25600	25619	CCAAATACCTAAAAGCTATT	84	1895
1102365	N/A	N/A	25601	25620	GCCAAATACCTAAAAGCTAT	108	1896
1102366	N/A	N/A	25602	25621	AGCCAAATACCTAAAAGCTA	86	1897
1102367	N/A	N/A	25603	25622	AAGCCAAATACCTAAAAGCT	71	1898
1102368	N/A	N/A	25604	25623	GAAGCCAAATACCTAAAAGC	54	1899
1102369	N/A	N/A	25605	25624	GGAAGCCAAATACCTAAAAG	44	1900
1102370	N/A	N/A	25632	25651	ACCCCTTGTAACTAAAAATA	93	1901
1102371	N/A	N/A	25689	25708	TGGCTAAAACTAATCATCTG	71	1902
1102372	N/A	N/A	25690	25709	ATGGCTAAAACTAATCATCT	70	1903
1102373	N/A	N/A	25691	25710	CATGGCTAAAACTAATCATC	98	1904
1102375	N/A	N/A	25805	25824	CATTACCCTTCATATATACA	73	1905
1102377	N/A	N/A	25814	25833	TCCTTAATACATTACCCTTC	62	1906
1102378	N/A	N/A	25822	25841	GTCGATACTCCTTAATACAT	23	1907
1102379	N/A	N/A	26243	26262	CTACAAATTATTGTTTCTGG	17	1908
1102380	N/A	N/A	26245	26264	GGCTACAAATTATTGTTTCT	25	1909

1102381	N/A	N/A	26246	26265	AGGCTACAAATTATTGTTTC	58	1910
1102382	N/A	N/A	26247	26266	AAGGCTACAAATTATTGTTT	50	1911
1102383	N/A	N/A	26249	26268	TGAAGGCTACAAATTATTGT	40	1912
1102384	N/A	N/A	26311	26330	ACTGTTAAACATATGATACT	73	1913
1102385	N/A	N/A	26322	26341	TCTTGGTTTCTACTGTTAAA	78	1914
1102386	N/A	N/A	26455	26474	AAAGGGCCCTACTAATATAG	107	1915
1102387	N/A	N/A	26475	26494	TGAGAAATAAATATGTCTGT	79	1916
1102388	N/A	N/A	26525	26544	CCTCACTTTCTCCATTGTAA	47	1917
1102389	N/A	N/A	26577	26596	TCTTATACTTACTAGTAAAG	77	1918
1102390	N/A	N/A	26580	26599	GATTCTTATACTTACTAGTA	70	1919
1102391	N/A	N/A	26581	26600	TGATTCTTATACTTACTAGT	92	1920
1102392	N/A	N/A	26584	26603	TAATGATTCTTATACTTACT	59	1921
1102393	N/A	N/A	26585	26604	ATAATGATTCTTATACTTAC	87	1922
1102394	N/A	N/A	26593	26612	TAGTCCAAATAATGATTCTT	50	1923
1102395	N/A	N/A	26629	26648	TGGAAAAAAATACAAGCTGA	88	1924
1102396	N/A	N/A	26630	26649	CTGGAAAAAAATACAAGCTG	68	1925
1102397	N/A	N/A	26631	26650	ACTGGAAAAAAATACAAGCT	84	1926
1102398	N/A	N/A	26632	26651	CACTGGAAAAAAATACAAGC	99	1927
1102399	N/A	N/A	26680	26699	GATTCAAAATTGATGTAAAA	95	1928
1102400	N/A	N/A	26681	26700	AGATTCAAAATTGATGTAAA	91	1929
1102401	N/A	N/A	26684	26703	AAGAGATTCAAAATTGATGT	124	1930
1102402	N/A	N/A	26685	26704	AAAGAGATTCAAAATTGATG	86	1931
1102403	N/A	N/A	26707	26726	AAAATCAACCTAACCAGTTA	87	1932
1102404	N/A	N/A	26708	26727	AAAAATCAACCTAACCAGTT	109	1933
1102405	N/A	N/A	26714	26733	AAAGGCAAAAATCAACCTAA	102	1934
1102406	N/A	N/A	26733	26752	ATAGAATAACCTAAAAAAAA	78	1935
1102407	N/A	N/A	26734	26753	TATAGAATAACCTAAAAAAA	131	1936
1102408	N/A	N/A	26737	26756	AAATATAGAATAACCTAAAA	102	1937
1102409	N/A	N/A	26739	26758	ACAAATATAGAATAACCTAA	95	1938
1102411	N/A	N/A	26870	26889	GGCCTCATTTTTACCTTTGC	85	1939
1102413	N/A	N/A	26898	26917	GAAATACTACCATATATTCC	89	1940
1102414	N/A	N/A	26923	26942	AGCATGAAAATTTAATTCTC	91	1941
1102415	N/A	N/A	26986	27005	TTCACTAAAATATAAGGTCC	73	1942
1102416	N/A	N/A	26995	27014	CTAATAAACTTCACTAAAAT	111	1943
1102417	N/A	N/A	26996	27015	ACTAATAAACTTCACTAAAA	70	1944
1102418	N/A	N/A	27008	27027	ATTCAAGTTTAAACTAATAA	85	1945
1102419	N/A	N/A	27027	27046	TAAGTATTTCAAAGAGTTGA	37	1946
1102420	N/A	N/A	27029	27048	TTTAAGTATTTCAAAGAGTT	110	1947
1102421	N/A	N/A	27036	27055	TAATATATTTAAGTATTTCA	82	1948
1102422	N/A	N/A	27043	27062	ACTAAGTTAATATATTTAAG	119	1949
1102423	N/A	N/A	27064	27083	AGGAATATACCATACCAGCT	34	1950
1102424	N/A	N/A	27066	27085	CTAGGAATATACCATACCAG	19	1951
1102425	N/A	N/A	27391	27410	CTAGTAATATAATGATTGTG	37	1952

1102426	N/A	N/A	27394	27413	GCTCTAGTAATATAATGATT	35	1953
1102427	N/A	N/A	27407	27426	TTCTGGCAAATAAGCTCTAG	44	1954
1102428	N/A	N/A	27470	27489	TTAGACATAACATAAAGGCA	68	1955
1102429	N/A	N/A	27481	27500	AATCTTCTATTTTAGACATA	93	1956
1102430	N/A	N/A	27486	27505	CAACCAATCTTCTATTTTAG	84	1957
1102431	N/A	N/A	27487	27506	GCAACCAATCTTCTATTTTA	83	1958
1102432	N/A	N/A	27492	27511	TAACTGCAACCAATCTTCTA	114	1959
1102433	N/A	N/A	27518	27537	ACTCTAAAGAACAAAAGCAC	85	1960
1102434	N/A	N/A	27523	27542	TATGGACTCTAAAGAACAAA	75	1961
1102435	N/A	N/A	27690	27709	GTCTTTACCTTGCATACTTA	65	1962
1102436	N/A	N/A	27697	27716	TCAGAATGTCTTTACCTTGC	104	1963
1102437	N/A	N/A	27712	27731	TGAATACAACACACATCAGA	81	1964
1102438	N/A	N/A	27718	27737	CAGCAATGAATACAACACAC	84	1965
1102439	N/A	N/A	27720	27739	TTCAGCAATGAATACAACAC	75	1966
1102440	N/A	N/A	27729	27748	AATCAATTCTTCAGCAATGA	100	1967
1102441	N/A	N/A	27730	27749	GAATCAATTCTTCAGCAATG	70	1968
1102442	N/A	N/A	27748	27767	GAAATCTAAGAATAATTGGA	108	1969
1102443	N/A	N/A	27763	27782	TACATTAACTTCCATGAAAT	91	1970
1102444	N/A	N/A	27770	27789	CTAAGAGTACATTAACTTCC	68	1971
1102445	N/A	N/A	27786	27805	AATTGTCAAAACACCTCTAA	77	1972
1102447	N/A	N/A	27824	27843	AAAGGGAAAGCCCACTATAT	118	1973
1102449	N/A	N/A	27848	27867	AGTGATTTCCATTATAAGAA	71	1974
1102450	N/A	N/A	27849	27868	AAGTGATTTCCATTATAAGA	69	1975
1102451	N/A	N/A	27872	27891	CCTAATAAAATATAGGTTGT	82	1976
1102452	N/A	N/A	27873	27892	TCCTAATAAAATATAGGTTG	108	1977
1102453	N/A	N/A	27874	27893	CTCCTAATAAAATATAGGTT	86	1978
1102454	N/A	N/A	27875	27894	ACTCCTAATAAAATATAGGT	166	1979
1102455	N/A	N/A	27882	27901	TATAACTACTCCTAATAAAA	82	1980
1102456	N/A	N/A	27885	27904	AAATATAACTACTCCTAATA	109	1981
1102457	N/A	N/A	27887	27906	AAAAATATAACTACTCCTAA	120	1982
1102458	N/A	N/A	27893	27912	AGGAGTAAAAATATAACTAC	117	1983
1102459	N/A	N/A	27894	27913	CAGGAGTAAAAATATAACTA	109	1984
1102460	N/A	N/A	27895	27914	CCAGGAGTAAAAATATAACT	91	1985
1102461	N/A	N/A	27903	27922	TAAAATAACCAGGAGTAAAA	88	1986
1102462	N/A	N/A	27908	27927	CCAAATAAAATAACCAGGAG	86	1987
1102463	N/A	N/A	27910	27929	AACCAAATAAAATAACCAGG	89	1988
1102464	N/A	N/A	27916	27935	TGTTGAAACCAAATAAAATA	108	1989
1102465	N/A	N/A	27943	27962	CCACAATTTACTATTGTGTT	96	1990
1102466	N/A	N/A	27947	27966	AAAACCACAATTTACTATTG	94	1991
1102467	N/A	N/A	27953	27972	AAGATTAAAACCACAATTTA	89	1992
1102468	N/A	N/A	27966	27985	ACTGATACCCACAAAGATTA	77	1993
1102469	N/A	N/A	27974	27993	AAGGGTCAACTGATACCCAC	89	1994
1102470	N/A	N/A	28007	28026	ATGGCACATATTTATGTAAC	51	1995

1102471	N/A	N/A	28083	28102	AGTTGCATAGCCAATAAATG	54	1996
1102472	N/A	N/A	28126	28145	TATCACTAAAAAACTGGGCC	100	1997
1102473	N/A	N/A	28127	28146	ATATCACTAAAAAACTGGGC	79	1998
1102474	N/A	N/A	28128	28147	TATATCACTAAAAAACTGGG	94	1999
1102475	N/A	N/A	28129	28148	TTATATCACTAAAAAACTGG	102	2000
1102476	N/A	N/A	28131	28150	GTTTATATCACTAAAAAACT	90	2001
1102477	N/A	N/A	28132	28151	AGTTTATATCACTAAAAAAC	146	2002
1102478	N/A	N/A	28133	28152	TAGTTTATATCACTAAAAAA	87	2003
1102479	N/A	N/A	28134	28153	ATAGTTTATATCACTAAAAA	101	2004
1102480	N/A	N/A	28136	28155	TGATAGTTTATATCACTAAA	99	2005
1102481	N/A	N/A	28138	28157	ATTGATAGTTTATATCACTA	94	2006
1102483	N/A	N/A	28195	28214	TGTCTTAACATTTTTCTTTG	47	2007
1102485	N/A	N/A	28229	28248	CACTTCAAACTTTTAATTAA	94	2008
1102486	N/A	N/A	28230	28249	CCACTTCAAACTTTTAATTA	80	2009
1102487	N/A	N/A	28233	28252	AACCCACTTCAAACTTTTAA	75	2010
1102488	N/A	N/A	28235	28254	AAAACCCACTTCAAACTTTT	83	2011
1102489	N/A	N/A	28271	28290	AAGCAAATACATATGAGTTA	59	2012
1102490	N/A	N/A	28273	28292	AGAAGCAAATACATATGAGT	24	2013
1102491	N/A	N/A	28274	28293	TAGAAGCAAATACATATGAG	83	2014
1102492	N/A	N/A	28288	28307	ATTTCATTAGAAAGTAGAAG	98	2015
1102493	N/A	N/A	28293	28312	AAATAATTTCATTAGAAAGT	97	2016
1102494	N/A	N/A	28297	28316	TGATAAATAATTTCATTAGA	95	2017
1102495	N/A	N/A	28340	28359	TTAATGAAATTTCAATTTTA	110	2018
1102496	N/A	N/A	28351	28370	TAATCTTCCCATTAATGAAA	85	2019
1102497	N/A	N/A	28355	28374	AAAATAATCTTCCCATTAAT	83	2020
1102498	N/A	N/A	28360	28379	GGATAAAAATAATCTTCCCA	79	2021
1102499	N/A	N/A	28361	28380	AGGATAAAAATAATCTTCCC	62	2022
1102500	N/A	N/A	28378	28397	AGAGGCAAGAAAAGTTCAGG	54	2023
1102501	N/A	N/A	28414	28433	GATTGCACACCATATGGAGT	63	2024
1102502	N/A	N/A	28431	28450	CTATTAATCAAAAATGGGAT	119	2025
1102503	N/A	N/A	28432	28451	TCTATTAATCAAAAATGGGA	79	2026
1102504	N/A	N/A	28434	28453	ACTCTATTAATCAAAAATGG	80	2027
1102505	N/A	N/A	28437	28456	AGGACTCTATTAATCAAAAA	77	2028
1102506	N/A	N/A	28439	28458	GCAGGACTCTATTAATCAAA	105	2029
1102507	N/A	N/A	28452	28471	CCCTGCTAATCCAGCAGGAC	130	2030
1102508	N/A	N/A	28477	28496	AAAGAAATCTAAAGCTGATT	115	2031
1102509	N/A	N/A	28810	28829	AGAATATTCTACTCTTCTGG	111	2032
1102510	N/A	N/A	28813	28832	TTAAGAATATTCTACTCTTC	103	2033
1102511	N/A	N/A	28817	28836	CTCTTTAAGAATATTCTACT	65	2034
1102512	N/A	N/A	28818	28837	TCTCTTTAAGAATATTCTAC	80	2035
1102513	N/A	N/A	28872	28891	TTCAAGCAACAATATGTTTG	86	2036
1102514	N/A	N/A	28880	28899	TTTACCAATTCAAGCAACAA	109	2037
1102515	N/A	N/A	28881	28900	ATTTACCAATTCAAGCAACA	128	2038

1102516	N/A	N/A	28883	28902	GTATTTACCAATTCAAGCAA	67	2039
1102517	N/A	N/A	28886	28905	ACTGTATTTACCAATTCAAG	86	2040
1102519	N/A	N/A	28895	28914	AAACCAATCACTGTATTTAC	126	2041
1102521	N/A	N/A	28902	28921	ACAACAAAAACCAATCACTG	100	2042
1102522	N/A	N/A	28903	28922	CACAACAAAAACCAATCACT	78	2043
1102523	N/A	N/A	28922	28941	ACCTGAAAACAAAACACAAC	95	2044
1102524	N/A	N/A	28923	28942	TACCTGAAAACAAAACACAA	25	2045
1102525	N/A	N/A	28926	28945	AACTACCTGAAAACAAAACA	78	2046
1102526	N/A	N/A	29022	29041	TTTACTTTTCAAAGTAGGCT	82	2047
1102527	N/A	N/A	29023	29042	CTTTACTTTTCAAAGTAGGC	109	2048
1102528	N/A	N/A	29025	29044	TACTTTACTTTTCAAAGTAG	109	2049
1102529	N/A	N/A	29028	29047	AACTACTTTACTTTTCAAAG	99	2050
1102530	N/A	N/A	29032	29051	TACCAACTACTTTACTTTTC	85	2051
1102531	N/A	N/A	29035	29054	TTGTACCAACTACTTTACTT	88	2052
1102532	N/A	N/A	29051	29070	AACATGCTACTTTAACTTGT	78	2053
1102533	N/A	N/A	29062	29081	AGCAAATATTAAACATGCTA	109	2054
1102534	N/A	N/A	29074	29093	CAAAATAGCCAAAGCAAATA	82	2055
1102535	N/A	N/A	29076	29095	GACAAAATAGCCAAAGCAAA	62	2056
1102536	N/A	N/A	29085	29104	TTACAAATAGACAAAATAGC	76	2057
1102537	N/A	N/A	29091	29110	AACCATTTACAAATAGACAA	63	2058
1102538	N/A	N/A	29096	29115	GCAGTAACCATTTACAAATA	42	2059
1102539	N/A	N/A	29119	29138	ATTCAAATATTCACAGGATT	55	2060
1102540	N/A	N/A	29125	29144	AAATACATTCAAATATTCAC	89	2061
1102541	N/A	N/A	29476	29495	GCCGTAAATTTTTATTTTTA	16	2062
1102542	N/A	N/A	29477	29496	TGCCGTAAATTTTTATTTTT	40	2063
1102543	N/A	N/A	29529	29548	GTTTAAAAAATTTATCCAGT	82	2064
1102544	N/A	N/A	29530	29549	AGTTTAAAAAATTTATCCAG	88	2065
1102545	N/A	N/A	29531	29550	CAGTTTAAAAAATTTATCCA	109	2066
1102546	N/A	N/A	29535	29554	CACTCAGTTTAAAAAATTTA	78	2067
1102547	N/A	N/A	29548	29567	ATAAGGTTTCCTTCACTCAG	22	2068
1102548	N/A	N/A	29561	29580	TAAATGAAATTTTATAAGGT	109	2069
1102549	N/A	N/A	29585	29604	GTCCTAATTTCATTTTTCTT	30	2070
1102550	N/A	N/A	29587	29606	TTGTCCTAATTTCATTTTTC	58	2071
1102551	N/A	N/A	29645	29664	AGGGTTAATCAGGTAAGCAA	8	2072
1102552	N/A	N/A	29647	29666	GCAGGGTTAATCAGGTAAGC	17	2073
1102553	N/A	N/A	29807	29826	TTGATCCAGATTTATGGTTT	28	2074
1102555	N/A	N/A	29812	29831	AGGAGTTGATCCAGATTTAT	28	2075
1102557	N/A	N/A	29881	29900	AATGTATTTTCATATGGTGG	10	2076
1102558	N/A	N/A	29901	29920	AATGATAGTTACTTGAAAAG	87	2077
1102559	N/A	N/A	30269	30288	TCTTGTAATCTTTAACATGA	84	2078
1102560	N/A	N/A	30280	30299	CTGATTATTTATCTTGTAAT	34	2079
1102561	N/A	N/A	30281	30300	TCTGATTATTTATCTTGTAA	34	2080
1102562	N/A	N/A	30282	30301	GTCTGATTATTTATCTTGTA	14	2081

1102563	N/A	N/A	30283	30302	GGTCTGATTATTTATCTTGT	15	2082
1102564	N/A	N/A	30350	30369	TGGATGAAATACAGCAAATA	42	2083
1102565	N/A	N/A	30354	30373	AGAATGGATGAAATACAGCA	82	2084
1102566	N/A	N/A	30376	30395	AATGTGAAACTATGTGCATC	57	2085
1102567	N/A	N/A	30378	30397	GAAATGTGAAACTATGTGCA	29	2086
1102568	N/A	N/A	30380	30399	TTGAAATGTGAAACTATGTG	58	2087
1102569	N/A	N/A	30398	30417	TTCTCAATTTCAGAGACATT	46	2088
1102570	N/A	N/A	30399	30418	CTTCTCAATTTCAGAGACAT	38	2089
1102571	N/A	N/A	30400	30419	GCTTCTCAATTTCAGAGACA	37	2090
1102572	N/A	N/A	30436	30455	GTGCTGCTAATATACTGTCA	26	2091
1102573	N/A	N/A	30452	30471	GAGCCAATATTTATAGGTGC	21	2092
1102574	N/A	N/A	30453	30472	TGAGCCAATATTTATAGGTG	7	2093
1102575	N/A	N/A	30473	30492	TTATACCATCAAATGTAAAA	83	2094
1102576	N/A	N/A	30475	30494	CATTATACCATCAAATGTAA	59	2095
1102577	N/A	N/A	30477	30496	TTCATTATACCATCAAATGT	53	2096
1102578	N/A	N/A	30478	30497	CTTCATTATACCATCAAATG	30	2097
1102579	N/A	N/A	30479	30498	TCTTCATTATACCATCAAAT	9	2098
1102580	N/A	N/A	30490	30509	GGTAAATATTTTCTTCATTA	9	2099
1102581	N/A	N/A	30495	30514	AAAAAGGTAAATATTTTCTT	84	2100
1102582	N/A	N/A	30520	30539	GTTGTGACTTAAAAACAAAA	74	2101
1102583	N/A	N/A	30523	30542	TGAGTTGTGACTTAAAAACA	49	2102
1102584	N/A	N/A	30546	30565	CAGAATTTTCCTTCATCTAC	89	2103
1102585	N/A	N/A	30547	30566	TCAGAATTTTCCTTCATCTA	42	2104
1102586	N/A	N/A	30548	30567	ATCAGAATTTTCCTTCATCT	34	2105
1102587	N/A	N/A	30574	30593	ATCTCACATTAAGAGGATGT	69	2106
1102588	N/A	N/A	30576	30595	ATATCTCACATTAAGAGGAT	69	2107
1102589	N/A	N/A	30577	30596	AATATCTCACATTAAGAGGA	41	2108
1102591	N/A	N/A	30582	30601	CTAGAAATATCTCACATTAA	88	2109
1102593	N/A	N/A	30587	30606	AAAGACTAGAAATATCTCAC	46	2110
1102594	N/A	N/A	30588	30607	TAAAGACTAGAAATATCTCA	65	2111
1102595	N/A	N/A	30600	30619	ATCTATACTGAATAAAGACT	72	2112
1102596	N/A	N/A	30605	30624	CATTAATCTATACTGAATAA	98	2113
1102597	N/A	N/A	30606	30625	CCATTAATCTATACTGAATA	64	2114
1102598	N/A	N/A	30607	30626	GCCATTAATCTATACTGAAT	19	2115
1102599	N/A	N/A	30608	30627	AGCCATTAATCTATACTGAA	7	2116
1102600	N/A	N/A	30609	30628	TAGCCATTAATCTATACTGA	25	2117
1102601	N/A	N/A	30610	30629	TTAGCCATTAATCTATACTG	80	2118
1102602	N/A	N/A	30611	30630	ATTAGCCATTAATCTATACT	65	2119
1102603	N/A	N/A	30613	30632	TAATTAGCCATTAATCTATA	66	2120
1102604	N/A	N/A	30614	30633	ATAATTAGCCATTAATCTAT	69	2121
1102605	N/A	N/A	30616	30635	ATATAATTAGCCATTAATCT	63	2122
1102606	N/A	N/A	30625	30644	AAATTTAACATATAATTAGC	89	2123
1102607	N/A	N/A	30632	30651	TACTTTGAAATTTAACATAT	92	2124

1102608	N/A	N/A	30651	30670	AAAAAGCACTAATAAGCACT	59	2125
1102609	N/A	N/A	30659	30678	TTAAAAGTAAAAAGCACTAA	91	2126
1102610	N/A	N/A	30675	30694	AAGTTAATTTTGAAACTTAA	118	2127
1102611	N/A	N/A	30697	30716	TTTGGAGTTTATTATAATAA	55	2128
1102612	N/A	N/A	30723	30742	TGCTAGTTTTTCTACTTTTG	13	2129
1102613	N/A	N/A	31103	31122	ATGGGAGTATTATAAAACGA	38	2130
1102614	N/A	N/A	31121	31140	CAGTGGAAAGAATGGGAGAT	48	2131
1102615	N/A	N/A	31147	31166	AAAATAATCCAAACTTGCAG	36	2132
1102616	N/A	N/A	31150	31169	TACAAAATAATCCAAACTTG	84	2133
1102617	N/A	N/A	31152	31171	GTTACAAAATAATCCAAACT	71	2134
1102618	N/A	N/A	31153	31172	TGTTACAAAATAATCCAAAC	82	2135
1102619	N/A	N/A	31154	31173	TTGTTACAAAATAATCCAAA	80	2136
1102620	N/A	N/A	31179	31198	TATAGAATAATATGATGATT	81	2137
1102621	N/A	N/A	31197	31216	GACACATATTAAAATGGTTA	25	2138
1102622	N/A	N/A	31237	31256	GCATTTAACTATGTTAAAAA	77	2139
1102623	N/A	N/A	31238	31257	AGCATTTAACTATGTTAAAA	88	2140
1102624	N/A	N/A	31240	31259	ATAGCATTTAACTATGTTAA	85	2141
1102625	N/A	N/A	31251	31270	ATTTTATGACAATAGCATTT	28	2142
1102627	N/A	N/A	31285	31304	TGATATAGAATTACAATTAA	112	2143
1102629	N/A	N/A	31647	31666	AAGTAGATTTAAGTTATTTT	118	2144
1102630	N/A	N/A	31650	31669	ATTAAGTAGATTTAAGTTAT	136	2145
1102631	N/A	N/A	31657	31676	TTTTCTAATTAAGTAGATTT	95	2146
1102632	N/A	N/A	31659	31678	GTTTTTCTAATTAAGTAGAT	103	2147
1102633	N/A	N/A	31660	31679	AGTTTTTCTAATTAAGTAGA	72	2148
1102634	N/A	N/A	31662	31681	TTAGTTTTTCTAATTAAGTA	123	2149
1102635	N/A	N/A	31664	31683	TGTTAGTTTTTCTAATTAAG	73	2150
1102636	N/A	N/A	32030	32049	TGCTTTAATTTCTATATTTC	71	2151
1102637	N/A	N/A	32676	32695	GCCAAAATACTAACATCAGT	110	2152
1102638	N/A	N/A	32677	32696	TGCCAAAATACTAACATCAG	42	2153
1102639	N/A	N/A	32678	32697	GTGCCAAAATACTAACATCA	26	2154
1102640	N/A	N/A	32679	32698	TGTGCCAAAATACTAACATC	52	2155
1102641	N/A	N/A	32680	32699	ATGTGCCAAAATACTAACAT	42	2156
1102642	N/A	N/A	32682	32701	GAATGTGCCAAAATACTAAC	36	2157
1102643	N/A	N/A	32683	32702	AGAATGTGCCAAAATACTAA	47	2158
1102644	N/A	N/A	32691	32710	ACAGAAAAAGAATGTGCCAA	48	2159
1102645	N/A	N/A	32726	32745	GAGTACAACACTTACAAGGT	24	2160
1102646	N/A	N/A	32750	32769	AGACTATTTACTGTCATAGG	15	2161
1102647	N/A	N/A	32752	32771	AAAGACTATTTACTGTCATA	54	2162
1102648	N/A	N/A	32754	32773	ACAAAGACTATTTACTGTCA	44	2163
1102649	N/A	N/A	32762	32781	AGCCTGTTACAAAGACTATT	64	2164
1102650	N/A	N/A	32777	32796	TATGAAATATCATGCAGCCT	47	2165
1102651	N/A	N/A	32778	32797	TTATGAAATATCATGCAGCC	63	2166
1102652	N/A	N/A	32786	32805	CATTCATTTTATGAAATATC	93	2167

1102653	N/A	N/A	32807	32826	ACATATAAATTATGCCACAT	49	2168
1102654	N/A	N/A	32826	32845	AGCAGAATTCAAAAGGCTCA	65	2169
1102655	N/A	N/A	32864	32883	GCAATATAAGAATTGTTCAT	19	2170
1102656	N/A	N/A	32933	32952	TCCTTTAACCCAATAATCTG	91	2171
1102657	N/A	N/A	32940	32959	GTTCATATCCTTTAACCCAA	8	2172
1102658	N/A	N/A	32975	32994	AGCAATTTAGAAATCTGTTC	68	2173
1102659	N/A	N/A	32993	33012	ATGGGAATTATTCTGGAAAG	40	2174
1102660	N/A	N/A	33005	33024	TGAAAGTATCACATGGGAAT	39	2175
1102661	N/A	N/A	33013	33032	AAACATGGTGAAAGTATCAC	33	2176
1102663	N/A	N/A	33370	33389	GATGTATGTCTTTAGACCAT	25	2177
1102665	N/A	N/A	33447	33466	GCAGTTTATTTTTATGCTTT	40	2178
1102666	N/A	N/A	33492	33511	GTTTCATATTTTTAATCCAG	7	2179
1102667	N/A	N/A	33497	33516	TGGAAGTTTCATATTTTTAA	14	2180
1102668	N/A	N/A	33498	33517	TTGGAAGTTTCATATTTTTA	18	2181
1102669	N/A	N/A	33875	33894	ACTTACTTAGTCATTATTGG	27	2182
1102670	N/A	N/A	33880	33899	TTATAACTTACTTAGTCATT	55	2183
1102671	N/A	N/A	33882	33901	TGTTATAACTTACTTAGTCA	27	2184
1102672	N/A	N/A	33884	33903	CTTGTTATAACTTACTTAGT	48	2185
1102673	N/A	N/A	33921	33940	TGTTTACTAAAAAGCACTAG	94	2186
1102674	N/A	N/A	33922	33941	CTGTTTACTAAAAAGCACTA	102	2187
1102675	N/A	N/A	33923	33942	CCTGTTTACTAAAAAGCACT	105	2188
1102676	N/A	N/A	33925	33944	ACCCTGTTTACTAAAAAGCA	110	2189
1102677	N/A	N/A	33956	33975	GAACATTTTTAAAAGGGTAC	13	2190
1102678	N/A	N/A	33957	33976	CGAACATTTTTAAAAGGGTA	15	2191
1102679	N/A	N/A	33959	33978	TTCGAACATTTTTAAAAGGG	22	2192
1102680	N/A	N/A	33973	33992	GAGGTATATCGATATTCGAA	41	2193
1102681	N/A	N/A	33993	34012	ATCCTCCACCAAGTAGGAAG	78	2194
1102682	N/A	N/A	34001	34020	CTCAATCAATCCTCCACCAA	97	2195
1102683	N/A	N/A	34014	34033	GCACACTTTCCTCCTCAATC	15	2196
1102684	N/A	N/A	34030	34049	GCTGGTAACCATCACTGCAC	12	2197
1102685	N/A	N/A	34031	34050	AGCTGGTAACCATCACTGCA	79	2198
1102686	N/A	N/A	34051	34070	AAGTCAAGCCAAGAGGCTGA	88	2199
1102687	N/A	N/A	34053	34072	CAAAGTCAAGCCAAGAGGCT	83	2200
1102688	N/A	N/A	34058	34077	ATTTGCAAAGTCAAGCCAAG	55	2201
1102689	N/A	N/A	34071	34090	AATTCTCACCAGTATTTGCA	45	2202
1102690	N/A	N/A	34082	34101	AGCTCTTTCCAAATTCTCAC	24	2203
1102691	N/A	N/A	34095	34114	TAAGATATTCTCAAGCTCTT	40	2204
1102692	N/A	N/A	34097	34116	TGTAAGATATTCTCAAGCTC	29	2205
1102693	N/A	N/A	34100	34119	CTATGTAAGATATTCTCAAG	58	2206
1102694	N/A	N/A	34102	34121	GACTATGTAAGATATTCTCA	31	2207
1102695	N/A	N/A	34111	34130	GCAACATGTGACTATGTAAG	16	2208
1102696	N/A	N/A	34130	34149	TAGTTCTTAACTCTTCTCAG	34	2209
1102697	N/A	N/A	34133	34152	AGTTAGTTCTTAACTCTTCT	39	2210

1102699	N/A	N/A	34147	34166	AATGAACATCAAGAAGTTAG	54	2211
1102701	N/A	N/A	34228	34247	AATTTTAGTGAAAGGCAAAT	84	2212
1102702	N/A	N/A	34235	34254	AATCAGGAATTTTAGTGAAA	53	2213
1102703	N/A	N/A	34241	34260	CTAAGTAATCAGGAATTTTA	106	2214
1102704	N/A	N/A	34277	34296	AAAGACAGAACCTAGAGAGA	83	2215
1102705	N/A	N/A	34287	34306	CCAAGCTCCCAAAGACAGAA	52	2216
1102706	N/A	N/A	34304	34323	GCTTGATAACCTTAGACCCA	37	2217
1102707	N/A	N/A	34402	34421	CAAATACTCAAAAAGGGAAA	47	2218
1102708	N/A	N/A	34403	34422	TCAAATACTCAAAAAGGGAA	75	2219
1102709	N/A	N/A	34405	34424	CTTCAAATACTCAAAAAGGG	107	2220
1102710	N/A	N/A	34406	34425	GCTTCAAATACTCAAAAAGG	45	2221
1102711	N/A	N/A	34407	34426	AGCTTCAAATACTCAAAAAG	69	2222
1102712	N/A	N/A	34411	34430	ATGAAGCTTCAAATACTCAA	71	2223
1102713	N/A	N/A	34424	34443	TACTATATTCAGTATGAAGC	33	2224
1102714	N/A	N/A	34425	34444	TTACTATATTCAGTATGAAG	59	2225
1102715	N/A	N/A	34427	34446	GATTACTATATTCAGTATGA	48	2226
1102716	N/A	N/A	34429	34448	ATGATTACTATATTCAGTAT	52	2227
1102717	N/A	N/A	34431	34450	CTATGATTACTATATTCAGT	31	2228
1102718	N/A	N/A	34432	34451	ACTATGATTACTATATTCAG	38	2229
1102719	N/A	N/A	34433	34452	TACTATGATTACTATATTCA	65	2230
1102720	N/A	N/A	34436	34455	GAATACTATGATTACTATAT	37	2231
1102721	N/A	N/A	34437	34456	TGAATACTATGATTACTATA	89	2232
1102722	N/A	N/A	34440	34459	GCATGAATACTATGATTACT	6	2233
1102723	N/A	N/A	34455	34474	TATGATTTTCTTTATGCATG	9	2234
1102724	N/A	N/A	34456	34475	TTATGATTTTCTTTATGCAT	29	2235
1102725	N/A	N/A	34465	34484	GCAATTACTTTATGATTTTC	12	2236
1102726	N/A	N/A	34467	34486	ATGCAATTACTTTATGATTT	15	2237
1102727	N/A	N/A	34468	34487	TATGCAATTACTTTATGATT	62	2238
1102728	N/A	N/A	34469	34488	TTATGCAATTACTTTATGAT	72	2239
1102729	N/A	N/A	34470	34489	TTTATGCAATTACTTTATGA	100	2240
1102730	N/A	N/A	34486	34505	ATGATTACTTTATGCATTTA	91	2241
1102731	N/A	N/A	34488	34507	CTATGATTACTTTATGCATT	57	2242
1102732	N/A	N/A	34493	34512	GAAAACTATGATTACTTTAT	83	2243
1102733	N/A	N/A	34494	34513	TGAAAACTATGATTACTTTA	65	2244
1102735	N/A	N/A	34498	34517	TGCATGAAAACTATGATTAC	59	2245
1102737	N/A	N/A	34511	34530	CTAGTTTTTTTAATGCATGA	34	2246
1102738	N/A	N/A	34512	34531	ACTAGTTTTTTTAATGCATG	76	2247
1102739	N/A	N/A	34513	34532	AACTAGTTTTTTTAATGCAT	74	2248
1102740	N/A	N/A	34851	34870	ATAAATTATGAATCTGTAAT	108	2249
1102741	N/A	N/A	34855	34874	ACTCATAAATTATGAATCTG	53	2250
1102742	N/A	N/A	34856	34875	GACTCATAAATTATGAATCT	86	2251
1102743	N/A	N/A	34857	34876	TGACTCATAAATTATGAATC	99	2252
1102744	N/A	N/A	34861	34880	TTAATGACTCATAAATTATG	101	2253

1102745	N/A	N/A	34877	34896	GGCTTGAAAATATTATTTAA	83	2254
1102746	N/A	N/A	34894	34913	GCTGGAAAAAATGTCATGGC	40	2255
1102747	N/A	N/A	34895	34914	TGCTGGAAAAAATGTCATGG	45	2256
1102748	N/A	N/A	34917	34936	GTAAAACAGATTTAGAGACT	68	2257
1102749	N/A	N/A	34919	34938	TGGTAAAACAGATTTAGAGA	36	2258
1102750	N/A	N/A	34971	34990	GGTTTTACAGTGACACAGCT	19	2259
1102751	N/A	N/A	35004	35023	TTGCTTAATTTCATGCTTCT	71	2260
1102752	N/A	N/A	35021	35040	AAATAGTTTCACACACATTG	27	2261
1102753	N/A	N/A	35023	35042	TAAAATAGTTTCACACACAT	63	2262
1102754	N/A	N/A	35025	35044	TATAAAATAGTTTCACACAC	69	2263
1102755	N/A	N/A	35061	35080	AACTGCCAACATGTATGTAT	42	2264
1102756	N/A	N/A	35094	35113	CATTTCAAAGCCACACCTAG	106	2265
1102757	N/A	N/A	35098	35117	CATCCATTTCAAAGCCACAC	44	2266
1102758	N/A	N/A	35174	35193	TGTCCATGAAGATATTTGTG	31	2267
1102759	N/A	N/A	35185	35204	ATAGCAATCCATGTCCATGA	10	2268
1102760	N/A	N/A	35186	35205	CATAGCAATCCATGTCCATG	22	2269
1102761	N/A	N/A	35187	35206	TCATAGCAATCCATGTCCAT	38	2270
1102762	N/A	N/A	35203	35222	TTAGGCAATCAAACACTCAT	73	2271
1102763	N/A	N/A	35240	35259	TAAATTATACCATATCACTG	88	2272
1102764	N/A	N/A	35243	35262	TGATAAATTATACCATATCA	110	2273
1102765	N/A	N/A	35247	35266	TGTTTGATAAATTATACCAT	79	2274
1102766	N/A	N/A	35264	35283	TTTCTGTTTCTCAACACTGT	77	2275
1102767	N/A	N/A	35286	35305	CTCTTTAAAACATCCCCAGT	95	2276
1102768	N/A	N/A	35290	35309	TTTCCTCTTTAAAACATCCC	37	2277
1102769	N/A	N/A	35321	35340	TATGTAAACCCCTAATTTCT	100	2278
1102771	N/A	N/A	35332	35351	TTTCTTAAGATTATGTAAAC	146	2279
1102773	N/A	N/A	35440	35459	TTTAATATCCTCATTACCCA	52	2280
1102774	N/A	N/A	35441	35460	ATTTAATATCCTCATTACCC	77	2281
1102775	N/A	N/A	35442	35461	AATTTAATATCCTCATTACC	71	2282
1102776	N/A	N/A	35446	35465	CTTAAATTTAATATCCTCAT	67	2283
1102777	N/A	N/A	35448	35467	TTCTTAAATTTAATATCCTC	75	2284
1102778	N/A	N/A	35450	35469	TGTTCTTAAATTTAATATCC	50	2285
1102779	N/A	N/A	35484	35503	GCTTTCTATGCCAAGGATCA	36	2286
1102780	N/A	N/A	35562	35581	AGTCCCAAAATTCTGCTTCA	127	2287
1102781	N/A	N/A	35566	35585	TGCCAGTCCCAAAATTCTGC	94	2288
1102782	N/A	N/A	35588	35607	GCAAGCAAAGCCATTTGGGA	80	2289
1102783	N/A	N/A	36442	36461	CTAAAAATACAAACCTTGTC	73	2290
1102784	N/A	N/A	36582	36601	CATGAGCTTTAAAAAGCAGA	153	2291
1102785	N/A	N/A	36603	36622	TGGTTACAAATTAAGTGCTC	79	2292
1102786	N/A	N/A	36604	36623	CTGGTTACAAATTAAGTGCT	64	2293
1102787	N/A	N/A	36606	36625	TTCTGGTTACAAATTAAGTG	37	2294
1102788	N/A	N/A	36624	36643	ATTATTTTACAAGTAGGATT	86	2295
1102789	N/A	N/A	36627	36646	TAGATTATTTTACAAGTAGG	15	2296

1102790	N/A	N/A	36628	36647	TTAGATTATTTTACAAGTAG	65	2297
1102791	N/A	N/A	36629	36648	CTTAGATTATTTTACAAGTA	55	2298
1102792	N/A	N/A	36634	36653	CATGTCTTAGATTATTTTAC	38	2299
1102793	N/A	N/A	36658	36677	TAGAGGTTACAAAGCTAAAA	31	2300
1102794	N/A	N/A	36670	36689	CCATCAATATTATAGAGGTT	7	2301
1102795	N/A	N/A	36734	36753	TCCAGCTGTGAAGACACTGA	103	2302
1102796	N/A	N/A	36757	36776	ACCTTGAAACAATGTAGACA	71	2303
1102797	N/A	N/A	36797	36816	ACTTTTAGTTTATGAAAAAT	96	2304
1102798	N/A	N/A	36799	36818	CTACTTTTAGTTTATGAAAA	105	2305
1102799	N/A	N/A	36804	36823	TTATTCTACTTTTAGTTTAT	75	2306
1102800	N/A	N/A	36807	36826	CCTTTATTCTACTTTTAGTT	53	2307
1102801	N/A	N/A	36808	36827	GCCTTTATTCTACTTTTAGT	22	2308
1102802	N/A	N/A	36811	36830	ATAGCCTTTATTCTACTTTT	17	2309
1102803	N/A	N/A	36815	36834	AGGAATAGCCTTTATTCTAC	57	2310
1102804	N/A	N/A	36817	36836	AGAGGAATAGCCTTTATTCT	51	2311
1102805	N/A	N/A	36830	36849	AGATAGCAATTTTAGAGGAA	30	2312
1102807	N/A	N/A	36973	36992	CCCATTAGCAAATCCTGATG	72	2313
1102809	N/A	N/A	37096	37115	AGAAAGTTCAACTAATGAGA	87	2314
1102810	N/A	N/A	37124	37143	TTTTGTGTTTTAAAACTGTG	61	2315
1102811	N/A	N/A	37153	37172	TGGCACATTTTTTATAGAGT	4	2316
1102812	N/A	N/A	37171	37190	CAACAATTATTAATAGAATG	81	2317
1102813	N/A	N/A	37172	37191	GCAACAATTATTAATAGAAT	77	2318
1102814	N/A	N/A	37173	37192	AGCAACAATTATTAATAGAA	109	2319
1102815	N/A	N/A	37174	37193	CAGCAACAATTATTAATAGA	48	2320
1102816	N/A	N/A	37176	37195	ACCAGCAACAATTATTAATA	55	2321
1102817	N/A	N/A	37177	37196	TACCAGCAACAATTATTAAT	106	2322
1102818	N/A	N/A	37185	37204	TTTTAAATTACCAGCAACAA	71	2323
1102819	N/A	N/A	37187	37206	ATTTTTAAATTACCAGCAAC	52	2324
1102820	N/A	N/A	37191	37210	AAGGATTTTTAAATTACCAG	35	2325
1102821	N/A	N/A	37194	37213	AACAAGGATTTTTAAATTAC	81	2326
1102822	N/A	N/A	37317	37336	GCTGACAATCTCAGTGAGAA	76	2327
1102823	N/A	N/A	37321	37340	AACAGCTGACAATCTCAGTG	58	2328
1102824	N/A	N/A	37330	37349	AAACTTACAAACAGCTGACA	66	2329
1102825	N/A	N/A	37332	37351	CAAAACTTACAAACAGCTGA	58	2330
1102826	N/A	N/A	37341	37360	ACCAAAAACCAAAACTTACA	89	2331
1102827	N/A	N/A	37342	37361	AACCAAAAACCAAAACTTAC	84	2332
1102828	N/A	N/A	37437	37456	CTAAAAAACCCCAAATCTAA	87	2333
1102829	N/A	N/A	37438	37457	CCTAAAAAACCCCAAATCTA	104	2334
1102830	N/A	N/A	37439	37458	TCCTAAAAAACCCCAAATCT	75	2335
1102831	N/A	N/A	37448	37467	ATTCACAAATCCTAAAAAAC	92	2336
1102832	N/A	N/A	37454	37473	GCAAATATTCACAAATCCTA	30	2337
1102833	N/A	N/A	37456	37475	GTGCAAATATTCACAAATCC	30	2338
1102834	N/A	N/A	37457	37476	AGTGCAAATATTCACAAATC	27	2339

1102835	N/A	N/A	37459	37478	ATAGTGCAAATATTCACAAA	33	2340
1102836	N/A	N/A	37535	37554	CATGATACTCAAAAGAGGTG	85	2341
1102837	N/A	N/A	37597	37616	CATCCTAAATCCGAGAATCA	100	2342
1102838	N/A	N/A	37601	37620	CAAGCATCCTAAATCCGAGA	90	2343
1102839	N/A	N/A	37618	37637	AATCTGAAATTACAGGTCAA	89	2344
1102840	N/A	N/A	37620	37639	TAAATCTGAAATTACAGGTC	90	2345
1102841	N/A	N/A	37633	37652	TTCTGCTTTTATGTAAATCT	20	2346
1102843	N/A	N/A	37711	37730	CATATTATTCCCAAATGGTT	53	2347
1102845	N/A	N/A	37762	37781	ACTTAGAAAATATACACTGA	82	2348
1102846	N/A	N/A	37764	37783	GTACTTAGAAAATATACACT	43	2349
1102847	N/A	N/A	37779	37798	TAGGAATATATTCTTGTACT	37	2350
1102848	N/A	N/A	37783	37802	TATGTAGGAATATATTCTTG	25	2351
1102849	N/A	N/A	37816	37835	TAAAATGTTTAAACATGACG	78	2352
1102850	N/A	N/A	37825	37844	TCCCCATTTTAAAATGTTTA	79	2353
1102851	N/A	N/A	37834	37853	TAATACAAATCCCCATTTTA	78	2354
1102852	N/A	N/A	37838	37857	AATGTAATACAAATCCCCAT	58	2355
1102853	N/A	N/A	37900	37919	ATCAGATTTTAAGTAATACT	85	2356
1102854	N/A	N/A	37903	37922	ATTATCAGATTTTAAGTAAT	87	2357
1102855	N/A	N/A	37906	37925	CACATTATCAGATTTTAAGT	69	2358
1102856	N/A	N/A	37907	37926	ACACATTATCAGATTTTAAG	48	2359
1102857	N/A	N/A	37908	37927	CACACATTATCAGATTTTAA	67	2360
1102858	N/A	N/A	37913	37932	TTTAACACACATTATCAGAT	67	2361
1102859	N/A	N/A	37917	37936	ACTATTTAACACACATTATC	85	2362
1102860	N/A	N/A	37919	37938	CTACTATTTAACACACATTA	65	2363
1102861	N/A	N/A	37922	37941	AAACTACTATTTAACACACA	60	2364
1102862	N/A	N/A	37923	37942	AAAACTACTATTTAACACAC	107	2365
1102863	N/A	N/A	37927	37946	AATGAAAACTACTATTTAAC	84	2366
1102864	N/A	N/A	38009	38028	TATCTTACTCATCTATTTCC	70	2367
1102865	N/A	N/A	38053	38072	TATTTCCCTCTTTATGGCAT	36	2368
1102866	N/A	N/A	38116	38135	CCCATTATTTCATCACTTCA	42	2369
1102867	N/A	N/A	38123	38142	TGACATTCCCATTATTTCAT	64	2370
1102868	N/A	N/A	38146	38165	CCATCCCACCAAAAGTAGCC	86	2371
1102869	N/A	N/A	38183	38202	AGCTTAAAATTTATCTCCCC	69	2372
1102870	N/A	N/A	38184	38203	GAGCTTAAAATTTATCTCCC	60	2373
1102871	N/A	N/A	38225	38244	ATAATGTTTCCATGGCTGGC	69	2374
1102872	N/A	N/A	38234	38253	TGAGTTAACATAATGTTTCC	45	2375
1102873	N/A	N/A	38236	38255	TGTGAGTTAACATAATGTTT	53	2376
1102874	N/A	N/A	38247	38266	TCAAACTACCATGTGAGTTA	93	2377
1102875	N/A	N/A	38251	38270	CATTTCAAACTACCATGTGA	101	2378
1102876	N/A	N/A	38252	38271	GCATTTCAAACTACCATGTG	46	2379
1102877	N/A	N/A	38255	38274	AAAGCATTTCAAACTACCAT	48	2380
1102879	N/A	N/A	38286	38305	AGTCACCAAAAATAAGTACC	66	2381
1102881	N/A	N/A	38294	38313	TTGTTGAAAGTCACCAAAAA	65	2382

1102882	N/A	N/A	38304	38323	ACCCTTAATATTGTTGAAAG	54	2383
1102883	N/A	N/A	38306	38325	AGACCCTTAATATTGTTGAA	53	2384
1102884	N/A	N/A	38311	38330	TTTATAGACCCTTAATATTG	82	2385
1102885	N/A	N/A	38357	38376	TACAAAAAGATTCACTGGTA	59	2386
1102886	N/A	N/A	38359	38378	CATACAAAAAGATTCACTGG	93	2387
1102887	N/A	N/A	38362	38381	TATCATACAAAAAGATTCAC	70	2388
1102888	N/A	N/A	38364	38383	CCTATCATACAAAAAGATTC	76	2389
1102889	N/A	N/A	38368	38387	AAAACCTATCATACAAAAAG	92	2390
1102890	N/A	N/A	38374	38393	AAACAAAAAACCTATCATAC	105	2391
1102891	N/A	N/A	38681	38700	AATAACCTATCATGGCCAGG	66	2392
1102892	N/A	N/A	38686	38705	CACAAAATAACCTATCATGG	94	2393
1102893	N/A	N/A	38687	38706	TCACAAAATAACCTATCATG	70	2394
1102894	N/A	N/A	38689	38708	CATCACAAAATAACCTATCA	75	2395
1102895	N/A	N/A	38690	38709	TCATCACAAAATAACCTATC	81	2396
1102896	N/A	N/A	38691	38710	TTCATCACAAAATAACCTAT	65	2397
1102897	N/A	N/A	38692	38711	TTTCATCACAAAATAACCTA	64	2398
1102898	N/A	N/A	38715	38734	CAGACAAATTAAGAGGTAGG	21	2399
1102899	N/A	N/A	38717	38736	ATCAGACAAATTAAGAGGTA	47	2400
1102900	N/A	N/A	38718	38737	TATCAGACAAATTAAGAGGT	48	2401
1102901	N/A	N/A	38724	38743	TAAATTTATCAGACAAATTA	106	2402
1102902	N/A	N/A	38726	38745	TTTAAATTTATCAGACAAAT	90	2403
1102903	N/A	N/A	38727	38746	ATTTAAATTTATCAGACAAA	62	2404
1102904	N/A	N/A	38730	38749	AAAATTTAAATTTATCAGAC	102	2405
1102905	N/A	N/A	38732	38751	ATAAAATTTAAATTTATCAG	115	2406
1102906	N/A	N/A	38736	38755	AGACATAAAATTTAAATTTA	106	2407
1102907	N/A	N/A	38738	38757	CTAGACATAAAATTTAAATT	89	2408
1102908	N/A	N/A	38773	38792	TACTTTAAAATATGGAAGTG	85	2409
1102909	N/A	N/A	38777	38796	AGATTACTTTAAAATATGGA	108	2410
1102910	N/A	N/A	38785	38804	TCTGATACAGATTACTTTAA	66	2411
1102911	N/A	N/A	38787	38806	AGTCTGATACAGATTACTTT	54	2412
1102912	N/A	N/A	38812	38831	GTATTAAAAGAATGCAAGAG	57	2413
1102913	N/A	N/A	38817	38836	CACTGGTATTAAAAGAATGC	66	2414
1102915	N/A	N/A	38852	38871	TAAGGAAAATACATTGTTTC	80	2415
1102917	N/A	N/A	38868	38887	TGAGAAAAACTATTCATAAG	86	2416
1102918	N/A	N/A	38869	38888	ATGAGAAAAACTATTCATAA	97	2417
1102919	N/A	N/A	38872	38891	ACCATGAGAAAAACTATTCA	64	2418
1102920	N/A	N/A	38879	38898	TAAATACACCATGAGAAAAA	101	2419
1102921	N/A	N/A	38880	38899	ATAAATACACCATGAGAAAA	68	2420
1102922	N/A	N/A	38882	38901	GAATAAATACACCATGAGAA	98	2421
1102923	N/A	N/A	38884	38903	AAGAATAAATACACCATGAG	98	2422
1102924	N/A	N/A	38885	38904	AAAGAATAAATACACCATGA	81	2423
1102925	N/A	N/A	38886	38905	AAAAGAATAAATACACCATG	109	2424
1102926	N/A	N/A	38890	38909	ACTTAAAAGAATAAATACAC	83	2425

1102927	N/A	N/A	38913	38932	GTGAAGTATATTTAAAAAAC	74	2426
1102928	N/A	N/A	38927	38946	TGAAACATTCAAAAGTGAAG	87	2427
1102929	N/A	N/A	38933	38952	GCTGTCTGAAACATTCAAAA	79	2428
1100520*	986	1005	38992	39011	ACTCTGTCCTGATAGGTCCC	17	2429
1100521*	988	1007	38994	39013	GAACTCTGTCCTGATAGGTC	12	2430
1100522*	1030	1049	39036	39055	CCAAGTGCTCCTGAACTGGT	19	2431
1100523*	1040	1059	39046	39065	TAGATCACTCCCAAGTGCTC	17	2432
1100524*	1043	1062	39049	39068	ACCTAGATCACTCCCAAGTG	16	2433
1100525*	1044	1063	N/A	N/A	CACCTAGATCACTCCCAAGT	18	2434
1100526*	1046	1065	N/A	N/A	ATCACCTAGATCACTCCCAA	20	2435
1100527*	1047	1066	N/A	N/A	CATCACCTAGATCACTCCCA	12	2436
1100528*	1049	1068	N/A	N/A	AGCATCACCTAGATCACTCC	10	2437
1100529*	1050	1069	N/A	N/A	TAGCATCACCTAGATCACTC	24	2438
1100530*	1052	1071	N/A	N/A	CATAGCATCACCTAGATCAC	21	2439
1100531*	1082	1101	45608	45627	CACAGCTGCCTGAAGCATGT	70	2440
1100532*	1083	1102	45609	45628	TCACAGCTGCCTGAAGCATG	19	2441
1100533*	1084	1103	45610	45629	GTCACAGCTGCCTGAAGCAT	15	2442
1100534*	1085	1104	45611	45630	GGTCACAGCTGCCTGAAGCA	4	2443
1100535*	1086	1105	45612	45631	TGGTCACAGCTGCCTGAAGC	6	2444
1100536*	1087	1106	45613	45632	ATGGTCACAGCTGCCTGAAG	13	2445
1100538*	1089	1108	45615	45634	ACATGGTCACAGCTGCCTGA	20	2446
1100540*	1091	1110	45617	45636	AGACATGGTCACAGCTGCCT	7	2447
1100541*	1092	1111	45618	45637	AAGACATGGTCACAGCTGCC	11	2448
1100542*	1093	1112	45619	45638	AAAGACATGGTCACAGCTGC	10	2449
1100543*	1094	1113	45620	45639	TAAAGACATGGTCACAGCTG	19	2450
1100544*	1095	1114	45621	45640	CTAAAGACATGGTCACAGCT	15	2451
1100545*	1098	1117	45624	45643	TTTCTAAAGACATGGTCACA	50	2452
1100546*	1099	1118	45625	45644	GTTTCTAAAGACATGGTCAC	19	2453
1100547*	1102	1121	45628	45647	ACAGTTTCTAAAGACATGGT	35	2454
1100548*	1103	1122	45629	45648	GACAGTTTCTAAAGACATGG	81	2455
1100549*	1104	1123	45630	45649	TGACAGTTTCTAAAGACATG	47	2456
1100550*	1105	1124	45631	45650	CTGACAGTTTCTAAAGACAT	34	2457
1100551*	1106	1125	45632	45651	TCTGACAGTTTCTAAAGACA	36	2458
1100552*	1111	1130	45637	45656	TCATTTCTGACAGTTTCTAA	24	2459
1100553*	1114	1133	45640	45659	AAATCATTTCTGACAGTTTC	29	2460
1100554*	1115	1134	45641	45660	CAAATCATTTCTGACAGTTT	27	2461
1100555*	1118	1137	45644	45663	TTTCAAATCATTTCTGACAG	28	2462
1100556*	1119	1138	45645	45664	TTTTCAAATCATTTCTGACA	53	2463
1102930*	N/A	N/A	39053	39072	CCTTACCTAGATCACTCCCA	52	2464
1102931*	N/A	N/A	39126	39145	AAAGCAAAAATCACATGGAG	58	2465
1102932*	N/A	N/A	39144	39163	GGGAATGAAGAATAATGTAA	24	2466
1102933*	N/A	N/A	39162	39181	TCTTAATATGATTAAAGAGG	61	2467
1102934*	N/A	N/A	39163	39182	TTCTTAATATGATTAAAGAG	100	2468

1102935*	N/A	N/A	39184	39203	AGATTACAAATTTACTTAAG	54	2469
1102936*	N/A	N/A	39185	39204	TAGATTACAAATTTACTTAA	116	2470
1102937*	N/A	N/A	39187	39206	AGTAGATTACAAATTTACTT	94	2471
1102938*	N/A	N/A	39192	39211	AATTTAGTAGATTACAAATT	85	2472
1102939*	N/A	N/A	39200	39219	TCCAGGGAAATTTAGTAGAT	16	2473
1102940*	N/A	N/A	39207	39226	TCCTTAATCCAGGGAAATTT	75	2474
1102941*	N/A	N/A	39213	39232	AACTGCTCCTTAATCCAGGG	22	2475
1102942*	N/A	N/A	39215	39234	GTAACTGCTCCTTAATCCAG	36	2476
1102943*	N/A	N/A	39307	39326	TTCTAGCAATCCTCTCCTGC	74	2477
1102944*	N/A	N/A	39339	39358	TTAAATTATTATGTTAAAGT	100	2478
1102945*	N/A	N/A	39340	39359	TTTAAATTATTATGTTAAAG	87	2479
1102946*	N/A	N/A	39341	39360	GTTTAAATTATTATGTTAAA	96	2480
1102947*	N/A	N/A	39342	39361	AGTTTAAATTATTATGTTAA	114	2481
1102948*	N/A	N/A	39343	39362	AAGTTTAAATTATTATGTTA	92	2482
1102949*	N/A	N/A	39344	39363	GAAGTTTAAATTATTATGTT	86	2483
1102951*	N/A	N/A	39347	39366	TGTGAAGTTTAAATTATTAT	98	2484
1102953*	N/A	N/A	39362	39381	GACTGTACAAATTACTGTGA	48	2485
1102954*	N/A	N/A	39364	39383	GAGACTGTACAAATTACTGT	67	2486
1102955*	N/A	N/A	39704	39723	TACTAATATTCATGATTTCT	66	2487
1102956*	N/A	N/A	39705	39724	CTACTAATATTCATGATTTC	76	2488
1102957*	N/A	N/A	39710	39729	TTCACCTACTAATATTCATG	35	2489
1102958*	N/A	N/A	39711	39730	TTTCACCTACTAATATTCAT	82	2490
1102959*	N/A	N/A	39713	39732	TTTTTCACCTACTAATATTC	82	2491
1102960*	N/A	N/A	39714	39733	ATTTTTCACCTACTAATATT	104	2492
1102961*	N/A	N/A	39753	39772	CTCAAGTATTTTTCATTTTC	72	2493
1102962*	N/A	N/A	39760	39779	GATTATACTCAAGTATTTTT	66	2494
1102963*	N/A	N/A	39762	39781	TAGATTATACTCAAGTATTT	66	2495
1102964*	N/A	N/A	39763	39782	TTAGATTATACTCAAGTATT	62	2496
1102965*	N/A	N/A	39764	39783	TTTAGATTATACTCAAGTAT	72	2497
1102966*	N/A	N/A	39767	39786	TTATTTAGATTATACTCAAG	79	2498
1102967*	N/A	N/A	39769	39788	TGTTATTTAGATTATACTCA	56	2499
1102968*	N/A	N/A	39774	39793	CCCATTGTTATTTAGATTAT	55	2500
1102969*	N/A	N/A	39815	39834	AGACATATTTAAACCGAGAC	15	2501
1102970*	N/A	N/A	39816	39835	AAGACATATTTAAACCGAGA	8	2502
1102971*	N/A	N/A	39817	39836	TAAGACATATTTAAACCGAG	16	2503
1102972*	N/A	N/A	39818	39837	TTAAGACATATTTAAACCGA	71	2504
1102973*	N/A	N/A	39833	39852	CTAATTGGCCAAAGTTTAAG	57	2505
1102974*	N/A	N/A	39844	39863	AACTTCTACTACTAATTGGC	37	2506
1102975*	N/A	N/A	39850	39869	TCTCTCAACTTCTACTACTA	39	2507
1102976*	N/A	N/A	39851	39870	TTCTCTCAACTTCTACTACT	60	2508
1102977*	N/A	N/A	39860	39879	AGTTACTTTTTCTCTCAACT	11	2509
1102978*	N/A	N/A	39883	39902	TGCTTATAATTTCTTTGTCA	10	2510
1102979*	N/A	N/A	39884	39903	CTGCTTATAATTTCTTTGTC	10	2511

1102980*	N/A	N/A	39885	39904	TCTGCTTATAATTTCTTTGT	11	2512
1102981*	N/A	N/A	39944	39963	CCTTCACCTTTTTATTGAGT	37	2513
1102982*	N/A	N/A	39952	39971	TTTCAAATCCTTCACCTTTT	43	2514
1102983*	N/A	N/A	39954	39973	CTTTTCAAATCCTTCACCTT	121	2515
1102984*	N/A	N/A	39958	39977	ATATCTTTTCAAATCCTTCA	44	2516
1102985*	N/A	N/A	40088	40107	TTCATTAAAGCCATACCTAC	88	2517
1102987*	N/A	N/A	40171	40190	TACACTTTTACATTCCCATT	16	2518
1102989*	N/A	N/A	40206	40225	TTATCAAAAAAATGCCAAAC	103	2519
1102990*	N/A	N/A	40207	40226	TTTATCAAAAAAATGCCAAA	111	2520
1102991*	N/A	N/A	40208	40227	ATTTATCAAAAAAATGCCAA	71	2521
1102992*	N/A	N/A	40210	40229	ACATTTATCAAAAAAATGCC	84	2522
1102993*	N/A	N/A	40211	40230	TACATTTATCAAAAAAATGC	80	2523
1102994*	N/A	N/A	40216	40235	AAGTATACATTTATCAAAAA	86	2524
1102995*	N/A	N/A	40284	40303	TATGTGAACCTAAGTTTTCT	61	2525
1102996*	N/A	N/A	40296	40315	GATATAAGTTTTTATGTGAA	34	2526
1102997*	N/A	N/A	40957	40976	AAGGTCTACATTTAGGCAGT	75	2527
1102998*	N/A	N/A	40979	40998	TTGTGCATTCATTAACTAAA	14	2528
1102999*	N/A	N/A	41041	41060	AGGAATAGAAAAAAGTACCA	58	2529
1103000*	N/A	N/A	41058	41077	GGCTGTACTTAAACAGGAGG	31	2530
1103001*	N/A	N/A	41083	41102	TTTTATACAAATGTTGAGGT	14	2531
1103002*	N/A	N/A	41085	41104	TGTTTTATACAAATGTTGAG	91	2532
1103003*	N/A	N/A	41089	41108	CTCATGTTTTATACAAATGT	64	2533
1103004*	N/A	N/A	41486	41505	AAGAAAATCCAGTCCACTCC	64	2534
1103005*	N/A	N/A	41488	41507	AAAAGAAAATCCAGTCCACT	56	2535
1103006*	N/A	N/A	41609	41628	TCTAAAGGTTTTTATCTTGC	31	2536
1103007*	N/A	N/A	41616	41635	CTTATTATCTAAAGGTTTTT	68	2537
1103008*	N/A	N/A	41731	41750	AGAAGTGTACCTTATGACTT	50	2538
1103009*	N/A	N/A	41812	41831	AGTGTTATCACCTCCTGGAG	106	2539
1103010*	N/A	N/A	41814	41833	GGAGTGTTATCACCTCCTGG	63	2540
1103011*	N/A	N/A	41881	41900	CAGAGAGATGCCTATGTATT	42	2541
1103012*	N/A	N/A	42140	42159	GGAGTGAAAGTCCAGGTTTC	30	2542
1103013*	N/A	N/A	42220	42239	CATCTTCCAATTTAGCAAGC	82	2543
1103014*	N/A	N/A	42232	42251	GAATCTTATTTACATCTTCC	12	2544
1103015*	N/A	N/A	42233	42252	TGAATCTTATTTACATCTTC	27	2545
1103016*	N/A	N/A	42234	42253	GTGAATCTTATTTACATCTT	28	2546
1103017*	N/A	N/A	42236	42255	ATGTGAATCTTATTTACATC	79	2547
1103018*	N/A	N/A	42280	42299	ATTTTCAATTAAATCCTGAA	66	2548
1103019*	N/A	N/A	42283	42302	GTGATTTTCAATTAAATCCT	70	2549
1103020*	N/A	N/A	42579	42598	CTGACACAAATTTAGATGGA	64	2550
1103021*	N/A	N/A	42764	42783	CAGTGTTCAGAAATCTGACT	87	2551
1103023*	N/A	N/A	42864	42883	CCTTCTGGCCTTTATGATCT	69	2552
1103025*	N/A	N/A	43501	43520	GAGAAATTCCTTTAGCCATT	16	2553
1103026*	N/A	N/A	43502	43521	AGAGAAATTCCTTTAGCCAT	28	2554

1103027*	N/A	N/A	43503	43522	TAGAGAAATTCCTTTAGCCA	19	2555
1103028*	N/A	N/A	43504	43523	TTAGAGAAATTCCTTTAGCC	30	2556
1103029*	N/A	N/A	43537	43556	CCAAAATTACTTCTTTTATC	46	2557
1103030*	N/A	N/A	43539	43558	TTCCAAAATTACTTCTTTTA	67	2558
1103031*	N/A	N/A	43540	43559	GTTCCAAAATTACTTCTTTT	15	2559
1103032*	N/A	N/A	43541	43560	TGTTCCAAAATTACTTCTTT	43	2560
1103033*	N/A	N/A	43542	43561	ATGTTCCAAAATTACTTCTT	95	2561
1103034*	N/A	N/A	43545	43564	CTGATGTTCCAAAATTACTT	52	2562
1103035*	N/A	N/A	43576	43595	TTTTACTCTTTTTATTGTTC	37	2563
1103036*	N/A	N/A	43582	43601	CCCATATTTTACTCTTTTTA	30	2564
1103037*	N/A	N/A	43584	43603	TACCCATATTTTACTCTTTT	50	2565
1103038*	N/A	N/A	43620	43639	TAGAAAATTCAAAAGGAGGG	90	2566
1103039*	N/A	N/A	43632	43651	CATCATACAATTTAGAAAAT	112	2567
1103040*	N/A	N/A	43642	43661	TTGCTTCAACCATCATACAA	56	2568
1103041*	N/A	N/A	43651	43670	CTATAATTCTTGCTTCAACC	19	2569
1103042*	N/A	N/A	43670	43689	ACTGAAAACCAAATCAGTGC	91	2570
1103043*	N/A	N/A	43672	43691	ATACTGAAAACCAAATCAGT	98	2571
1103044*	N/A	N/A	43675	43694	TATATACTGAAAACCAAATC	156	2572
1103045*	N/A	N/A	43693	43712	CCTTAAATATTTCCAATATA	73	2573
1103046*	N/A	N/A	43699	43718	ATAATGCCTTAAATATTTCC	33	2574
1103047*	N/A	N/A	43734	43753	CCCTTTATATCCTTTGACCC	46	2575
1103048*	N/A	N/A	43741	43760	GTTACCTCCCTTTATATCCT	32	2576
1103049*	N/A	N/A	43744	43763	AAGGTTACCTCCCTTTATAT	69	2577
1103050*	N/A	N/A	43746	43765	GAAAGGTTACCTCCCTTTAT	82	2578
1103051*	N/A	N/A	43747	43766	AGAAAGGTTACCTCCCTTTA	73	2579
1103052*	N/A	N/A	43755	43774	AGAAATATAGAAAGGTTACC	93	2580
1103053*	N/A	N/A	43768	43787	GCATCAGTACAAAAGAAATA	86	2581
1103054*	N/A	N/A	43795	43814	ATAGTGAAATTATTTTCCAA	53	2582
1103055*	N/A	N/A	43807	43826	GTTTTTAAACAAATAGTGAA	95	2583
1103056*	N/A	N/A	43811	43830	TTCAGTTTTTAAACAAATAG	91	2584
1103057*	N/A	N/A	43812	43831	GTTCAGTTTTTAAACAAATA	48	2585
1103059*	N/A	N/A	44052	44071	TTCAGCAATTAAAGACTTTT	48	2586
1103061*	N/A	N/A	44073	44092	CAAATATTAGCCAAAGAGGC	90	2587
1103062*	N/A	N/A	44396	44415	ATAATGATCTTCCAGGCTGG	138	2588
1103063*	N/A	N/A	44400	44419	CTAAATAATGATCTTCCAGG	105	2589
1103064*	N/A	N/A	44404	44423	AGGACTAAATAATGATCTTC	45	2590
1103065*	N/A	N/A	44548	44567	ATATAAATTTCTATTTTTGG	81	2591
1103066*	N/A	N/A	44549	44568	AATATAAATTTCTATTTTTG	112	2592
1103067*	N/A	N/A	44674	44693	CAGTAGAGTATTACATGCTA	29	2593
1103068*	N/A	N/A	44688	44707	CTTTTTAATCCTGACAGTAG	63	2594
1103069*	N/A	N/A	44693	44712	GGTTTCTTTTTAATCCTGAC	89	2595
1103070*	N/A	N/A	44695	44714	TGGGTTTCTTTTTAATCCTG	76	2596
1103071*	N/A	N/A	44733	44752	CCCCTGAGATCCAGCCACGG	90	2597

1103072*	N/A	N/A	44809	44828	AGCTGTCATTTTTAGTTGAA	31	2598
1103073*	N/A	N/A	44826	44845	GTTCTCTATCTCTATACAGC	19	2599
1103074*	N/A	N/A	44844	44863	AGTGGAAACCACTAATATGT	79	2600
1103075*	N/A	N/A	44861	44880	ACCCACTTTCTCTAACTAGT	69	2601
1103076*	N/A	N/A	44897	44916	CTGCTATCGATTTATATTCC	99	2602
1103077*	N/A	N/A	44920	44939	GTTATAATACCACAAAGATC	26	2603
1103078*	N/A	N/A	44921	44940	TGTTATAATACCACAAAGAT	80	2604
1103079*	N/A	N/A	44923	44942	AGTGTTATAATACCACAAAG	52	2605
1103080*	N/A	N/A	44924	44943	AAGTGTTATAATACCACAAA	76	2606
1103081*	N/A	N/A	44925	44944	GAAGTGTTATAATACCACAA	33	2607
1103082*	N/A	N/A	44932	44951	AGACATAGAAGTGTTATAAT	61	2608
1103083*	N/A	N/A	44940	44959	TACAATCAAGACATAGAAGT	76	2609
1103084*	N/A	N/A	44984	45003	TACATGGCATTTTATCACAC	32	2610
1103085*	N/A	N/A	44997	45016	TTATATGTAGTTCTACATGG	62	2611
1103086*	N/A	N/A	45032	45051	CAAACTAAAACCTAGATATT	90	2612
1103087*	N/A	N/A	45035	45054	GATCAAACTAAAACCTAGAT	76	2613
1103088*	N/A	N/A	45036	45055	AGATCAAACTAAAACCTAGA	91	2614
1103089*	N/A	N/A	45038	45057	AAAGATCAAACTAAAACCTA	74	2615
1103090*	N/A	N/A	45041	45060	ACTAAAGATCAAACTAAAAC	101	2616
1103091*	N/A	N/A	45043	45062	TAACTAAAGATCAAACTAAA	113	2617
1103092*	N/A	N/A	45044	45063	GTAACTAAAGATCAAACTAA	100	2618
1103093*	N/A	N/A	45077	45096	TTTGCCCAATTTCACCCAAT	46	2619
1103095*	N/A	N/A	45114	45133	AGTTGTAAAGATATTTAAGA	86	2620
1103097*	N/A	N/A	45155	45174	AAACCCAACTTTCTATTTTG	57	2621
1103098*	N/A	N/A	45161	45180	TTACAAAAACCCAACTTTCT	86	2622
1103099*	N/A	N/A	45162	45181	TTTACAAAAACCCAACTTTC	79	2623
1103100*	N/A	N/A	45165	45184	GTATTTACAAAAACCCAACT	45	2624
1103101*	N/A	N/A	45167	45186	ATGTATTTACAAAAACCCAA	57	2625
1103102*	N/A	N/A	45172	45191	AATTCATGTATTTACAAAAA	76	2626
1103103*	N/A	N/A	45184	45203	GTGTATATCAACAATTCATG	8	2627
1103104*	N/A	N/A	45186	45205	TTGTGTATATCAACAATTCA	65	2628
1103105*	N/A	N/A	45313	45332	GATAGCCACCAGTATATTCT	75	2629
1103106*	N/A	N/A	45316	45335	CCAGATAGCCACCAGTATAT	41	2630
1103107*	N/A	N/A	45332	45351	TCCCCATTTCCTAATCCCAG	96	2631
1103108*	N/A	N/A	45370	45389	CCCCAGAAAATTCCCCCATG	85	2632
1103109*	N/A	N/A	45390	45409	GATACACAACCATTCCATTG	68	2633
1103110*	N/A	N/A	45395	45414	ATCAAGATACACAACCATTC	63	2634
1103111*	N/A	N/A	45410	45429	TTTGACAAATACACCATCAA	68	2635
1103112*	N/A	N/A	45421	45440	GTTCTATATATTTTGACAAA	47	2636
1103113*	N/A	N/A	45423	45442	TAGTTCTATATATTTTGACA	38	2637
1103114*	N/A	N/A	45426	45445	TTATAGTTCTATATATTTTG	73	2638
1103115*	N/A	N/A	45430	45449	ACTTTTATAGTTCTATATAT	104	2639
1103116*	N/A	N/A	45473	45492	CACGAGTTTCTTTTTTTGAT	20	2640

1103117*	N/A	N/A	45491	45510	AATGTATTTCTATTTGAGCA	40	2641
1103118*	N/A	N/A	45520	45539	CAAAGTCATCAAAAGGCAAG	86	2642
1103119*	N/A	N/A	45525	45544	ATTCTCAAAGTCATCAAAAG	84	2643
1103120*	N/A	N/A	45529	45548	GAAAATTCTCAAAGTCATCA	99	2644
1103121*	N/A	N/A	45534	45553	TTCCAGAAAATTCTCAAAGT	95	2645
1103122*	N/A	N/A	45548	45567	CATTTCTTTAAAATTTCCAG	92	2646
1103123*	N/A	N/A	45552	45571	ACCACATTTCTTTAAAATTT	88	2647
1103124*	N/A	N/A	45559	45578	AAACAAAACCACATTTCTTT	102	2648
1103125*	N/A	N/A	45560	45579	GAAACAAAACCACATTTCTT	100	2649
1103126*	N/A	N/A	45561	45580	GGAAACAAAACCACATTTCT	108	2650
1103127*	N/A	N/A	45562	45581	GGGAAACAAAACCACATTTC	80	2651
1103128*	N/A	N/A	45564	45583	TTGGGAAACAAAACCACATT	100	2652
1103129*	N/A	N/A	45565	45584	GTTGGGAAACAAAACCACAT	94	2653

Table 3

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	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')	ATXN3 (% control)	SEQ ID NO
1100368	312	331	16178	16197	CCCAAACTTTCAAGGCATTG	31	169
1100368	312	331	16178	16197	CCCAAACTTTCAAGGCATTG	30	169
1100404	407	426	16700	16719	GTGTTCCTTATAATTGCATA	32	203
1100404	407	426	16700	16719	GTGTTCCTTATAATTGCATA	31	203
1100440	515	534	21242	21261	TAATTGAGCCAAGAAAAGTG	96	237
1100440	515	534	21242	21261	TAATTGAGCCAAGAAAAGTG	130	237
1100476	711	730	27568	27587	TTCCTGAGCCATCATTTGCT	62	271
1100476	711	730	27568	27587	TTCCTGAGCCATCATTTGCT	71	271
1100512	886	905	28981	29000	TCTGAAGTAAGATTTGTACC	57	305
1100512	886	905	28981	29000	TCTGAAGTAAGATTTGTACC	95	305
1100548	1103	1122	45629	45648	GACAGTTTCTAAAGACATGG	62	2455
1100584	1244	1263	45770	45789	AAGTCTTATTTCCTCATCTC	18	338
1100584	1244	1263	45770	45789	AAGTCTTATTTCCTCATCTC	16	338
1100620	1619	1638	46145	46164	GAACCATTACTATTATCAAC	31	372
1100620	1619	1638	46145	46164	GAACCATTACTATTATCAAC	35	372
1100656	1807	1826	46333	46352	AGTCATGAAATAATGATCCC	76	406
1100656	1807	1826	46333	46352	AGTCATGAAATAATGATCCC	59	406
1100692	2047	2066	46573	46592	TAGTCTTCTAACAGAAGGAG	81	440
1100728	2236	2255	46762	46781	TCATGTTCCAGATCACCATC	38	474
1100728	2236	2255	46762	46781	TCATGTTCCAGATCACCATC	34	474
1100764	2386	2405	46912	46931	AATTAAAGAGAATATTTATC	95	508
1100764	2386	2405	46912	46931	AATTAAAGAGAATATTTATC	96	508

1100800	2570	2589	47096	47115	GAAGTTGTCAGCTGAAATTT	35	542
1100800	2570	2589	47096	47115	GAAGTTGTCAGCTGAAATTT	38	542
1100836	2744	2763	47270	47289	AATGACTTAAAAAATCTGTT	84	576
1100836	2744	2763	47270	47289	AATGACTTAAAAAATCTGTT	85	576
1100872	2927	2946	47453	47472	CAGTCTTAAAATATTTAGCT	19	610
1100872	2927	2946	47453	47472	CAGTCTTAAAATATTTAGCT	14	610
1100908	3062	3081	47588	47607	TCTCATTTTTATATTAGGTA	31	644
1100908	3062	3081	47588	47607	TCTCATTTTTATATTAGGTA	20	644
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	8	45
1100914	3074	3093	47600	47619	GCATATTGGTTTTCTCATTT	9	45
1100945	3555	3574	48081	48100	TCACAACAAACTACACAAAC	77	678
1100945	3555	3574	48081	48100	TCACAACAAACTACACAAAC	70	678
1100981	3682	3701	48208	48227	CTGGCATCTTTTCATACTGG	37	712
1100981	3682	3701	48208	48227	CTGGCATCTTTTCATACTGG	33	712
1101017	3874	3893	48400	48419	TATTAAACATTAAGATGTTC	78	746
1101017	3874	3893	48400	48419	TATTAAACATTAAGATGTTC	88	746
1101053	3935	3954	48461	48480	GTACATACTTGATCCCAGTA	20	780
1101053	3935	3954	48461	48480	GTACATACTTGATCCCAGTA	16	780
1101089	4022	4041	48548	48567	AAAACATAAATTACTCATTA	102	814
1101089	4022	4041	48548	48567	AAAACATAAATTACTCATTA	100	814
1101125	4170	4189	48696	48715	AATTGTAAATTATTTGGCCA	78	848
1101125	4170	4189	48696	48715	AATTGTAAATTATTTGGCCA	62	848
1101161	4834	4853	49360	49379	CTACTTAAGATTTTAAAATT	96	882
1101161	4834	4853	49360	49379	CTACTTAAGATTTTAAAATT	137	882
1101197	5992	6011	50518	50537	TAATTAGGGTCACATATATA	70	916
1101197	5992	6011	50518	50537	TAATTAGGGTCACATATATA	113	916
1101233	6228	6247	50754	50773	ATCAAAATTCTAGAATTTAC	92	950
1101233	6228	6247	50754	50773	ATCAAAATTCTAGAATTTAC	72	950
1101269	6563	6582	51089	51108	CAGTGTTGTAAAAATTAGAT	81	984
1101269	6563	6582	51089	51108	CAGTGTTGTAAAAATTAGAT	78	984
1101305	6764	6783	51290	51309	GTGTGTGTAATAACAGCAAA	75	1018
1101305	6764	6783	51290	51309	GTGTGTGTAATAACAGCAAA	89	1018
1101341	96	115	13165	13184	GAGCACAAAGTGAGCCTTCT	60	1052
1101341	96	115	13165	13184	GAGCACAAAGTGAGCCTTCT	91	1052
1101377	229	248	13298	13317	GTGCGATAATCTTCACTAGT	82	1086
1101377	229	248	13298	13317	GTGCGATAATCTTCACTAGT	85	1086
1101413	N/A	N/A	51449	51468	ACACAAATTCAAAAGGAAAT	91	1116
1101413	N/A	N/A	51449	51468	ACACAAATTCAAAAGGAAAT	85	1116
1101593	N/A	N/A	4174	4193	CACTCCTAATACCTAAAAAC	97	1166
1101593	N/A	N/A	4174	4193	CACTCCTAATACCTAAAAAC	119	1166
1101629	N/A	N/A	5365	5384	GCCTTTGAAAATTAATAACA	89	1200
1101629	N/A	N/A	5365	5384	GCCTTTGAAAATTAATAACA	86	1200
1101665	N/A	N/A	6667	6686	TGACAGAGACTACAGCTGGC	91	1234

1101665	N/A	N/A	6667	6686	TGACAGAGACTACAGCTGGC	76	1234
1101701	N/A	N/A	7486	7505	ACACTACTAACTACAACACA	87	1268
1101701	N/A	N/A	7486	7505	ACACTACTAACTACAACACA	117	1268
1101737	N/A	N/A	8823	8842	TCAGTACAAATTTAAAAATC	84	1302
1101737	N/A	N/A	8823	8842	TCAGTACAAATTTAAAAATC	102	1302
1101773	N/A	N/A	9341	9360	TTCCAGTCACAAAAGCTCAA	59	1336
1101773	N/A	N/A	9341	9360	TTCCAGTCACAAAAGCTCAA	57	1336
1101809	N/A	N/A	10463	10482	TACTGAATAATATGCAAATT	107	1370
1101809	N/A	N/A	10463	10482	TACTGAATAATATGCAAATT	98	1370
1101845	N/A	N/A	11711	11730	CCCTAGAACATTTATTCTTT	84	1404
1101845	N/A	N/A	11711	11730	CCCTAGAACATTTATTCTTT	86	1404
1101881	N/A	N/A	13129	13148	AGAAAAAATTAAAATGTGAC	80	1438
1101881	N/A	N/A	13129	13148	AGAAAAAATTAAAATGTGAC	105	1438
1101917	N/A	N/A	14390	14409	AAGGAATTTTTAAATGCCCC	70	1472
1101917	N/A	N/A	14390	14409	AAGGAATTTTTAAATGCCCC	72	1472
1101953	N/A	N/A	15441	15460	CTGGGCATTTAAACTGAAGG	59	1506
1101953	N/A	N/A	15441	15460	CTGGGCATTTAAACTGAAGG	46	1506
1101989	N/A	N/A	16110	16129	CCATTCCAAATTTAGGAAGT	92	1540
1101989	N/A	N/A	16110	16129	CCATTCCAAATTTAGGAAGT	73	1540
1102025	N/A	N/A	17173	17192	TTCCTAATTTTAAAGTCAGC	33	1574
1102025	N/A	N/A	17173	17192	TTCCTAATTTTAAAGTCAGC	43	1574
1102061	N/A	N/A	17584	17603	CTTGCTCAAGACATATTTCA	60	1608
1102061	N/A	N/A	17584	17603	CTTGCTCAAGACATATTTCA	52	1608
1102097	N/A	N/A	19126	19145	CCAGAGGTTAAATAATCTCA	56	1642
1102097	N/A	N/A	19126	19145	CCAGAGGTTAAATAATCTCA	47	1642
1102133	N/A	N/A	19460	19479	ACAATGTTAATACTTTTTCC	50	1676
1102133	N/A	N/A	19460	19479	ACAATGTTAATACTTTTTCC	63	1676
1102169	N/A	N/A	20122	20141	TGTCAAAAGATTCCAATTGT	65	1710
1102169	N/A	N/A	20122	20141	TGTCAAAAGATTCCAATTGT	62	1710
1102205	N/A	N/A	21101	21120	TTAAGAATAGATACAACCCA	80	1744
1102205	N/A	N/A	21101	21120	TTAAGAATAGATACAACCCA	89	1744
1102241	N/A	N/A	22464	22483	TTTATGTTATTTTTTAGCCA	86	1778
1102241	N/A	N/A	22464	22483	TTTATGTTATTTTTTAGCCA	77	1778
1102277	N/A	N/A	23289	23308	AGAGACAATCCTAAGGAAAA	83	1812
1102277	N/A	N/A	23289	23308	AGAGACAATCCTAAGGAAAA	90	1812
1102313	N/A	N/A	24093	24112	TTAGGAAAACCACAGCATGG	84	1846
1102313	N/A	N/A	24093	24112	TTAGGAAAACCACAGCATGG	78	1846
1102349	N/A	N/A	25507	25526	CCAGAAATCCAGGGTTTCCC	62	1880
1102349	N/A	N/A	25507	25526	CCAGAAATCCAGGGTTTCCC	92	1880
1102385	N/A	N/A	26322	26341	TCTTGGTTTCTACTGTTAAA	21	1914
1102385	N/A	N/A	26322	26341	TCTTGGTTTCTACTGTTAAA	22	1914
1102421	N/A	N/A	27036	27055	TAATATATTTAAGTATTTCA	77	1948
1102421	N/A	N/A	27036	27055	TAATATATTTAAGTATTTCA	115	1948

1102457	N/A	N/A	27887	27906	AAAAATATAACTACTCCTAA	83	1982
1102457	N/A	N/A	27887	27906	AAAAATATAACTACTCCTAA	59	1982
1102493	N/A	N/A	28293	28312	AAATAATTTCATTAGAAAGT	89	2016
1102493	N/A	N/A	28293	28312	AAATAATTTCATTAGAAAGT	80	2016
1102529	N/A	N/A	29028	29047	AACTACTTTACTTTTCAAAG	81	2050
1102529	N/A	N/A	29028	29047	AACTACTTTACTTTTCAAAG	104	2050
1102565	N/A	N/A	30354	30373	AGAATGGATGAAATACAGCA	53	2084
1102565	N/A	N/A	30354	30373	AGAATGGATGAAATACAGCA	81	2084
1102601	N/A	N/A	30610	30629	TTAGCCATTAATCTATACTG	34	2118
1102601	N/A	N/A	30610	30629	TTAGCCATTAATCTATACTG	32	2118
1102637	N/A	N/A	32676	32695	GCCAAAATACTAACATCAGT	25	2152
1102637	N/A	N/A	32676	32695	GCCAAAATACTAACATCAGT	33	2152
1102673	N/A	N/A	33921	33940	TGTTTACTAAAAAGCACTAG	65	2186
1102673	N/A	N/A	33921	33940	TGTTTACTAAAAAGCACTAG	98	2186
1102709	N/A	N/A	34405	34424	CTTCAAATACTCAAAAAGGG	63	2220
1102709	N/A	N/A	34405	34424	CTTCAAATACTCAAAAAGGG	63	2220
1102745	N/A	N/A	34877	34896	GGCTTGAAAATATTATTTAA	83	2254
1102745	N/A	N/A	34877	34896	GGCTTGAAAATATTATTTAA	89	2254
1102781	N/A	N/A	35566	35585	TGCCAGTCCCAAAATTCTGC	83	2288
1102781	N/A	N/A	35566	35585	TGCCAGTCCCAAAATTCTGC	95	2288
1102817	N/A	N/A	37177	37196	TACCAGCAACAATTATTAAT	67	2322
1102817	N/A	N/A	37177	37196	TACCAGCAACAATTATTAAT	68	2322
1102853	N/A	N/A	37900	37919	ATCAGATTTTAAGTAATACT	66	2356
1102853	N/A	N/A	37900	37919	ATCAGATTTTAAGTAATACT	94	2356
1102889	N/A	N/A	38368	38387	AAAACCTATCATACAAAAAG	95	2390
1102889	N/A	N/A	38368	38387	AAAACCTATCATACAAAAAG	108	2390
1102925	N/A	N/A	38886	38905	AAAAGAATAAATACACCATG	84	2424
1102925	N/A	N/A	38886	38905	AAAAGAATAAATACACCATG	102	2424
1102961	N/A	N/A	39753	39772	CTCAAGTATTTTTCATTTTC	45	2493
1102997	N/A	N/A	40957	40976	AAGGTCTACATTTAGGCAGT	38	2527
1103033	N/A	N/A	43542	43561	ATGTTCCAAAATTACTTCTT	52	2561
1103069	N/A	N/A	44693	44712	GGTTTCTTTTTAATCCTGAC	13	2595
1103105	N/A	N/A	45313	45332	GATAGCCACCAGTATATTCT	32	2629
1100548*	1103	1122	45629	45648	GACAGTTTCTAAAGACATGG	47	2455
1100692*	2047	2066	46573	46592	TAGTCTTCTAACAGAAGGAG	58	440
1102961*	N/A	N/A	39753	39772	CTCAAGTATTTTTCATTTTC	46	2493
1102997*	N/A	N/A	40957	40976	AAGGTCTACATTTAGGCAGT	34	2527
1103033*	N/A	N/A	43542	43561	ATGTTCCAAAATTACTTCTT	50	2561
1103069*	N/A	N/A	44693	44712	GGTTTCTTTTTAATCCTGAC	14	2595
1103105*	N/A	N/A	45313	45332	GATAGCCACCAGTATATTCT	35	2629

Table 4

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	SEQ ID No: 3 Start Site	SEQ ID No: 3 Stop Site	Sequence (5' to 3')	ATXN3 (% control)	SEQ ID NO
1100366	88	107	GCATTGCTTATAACTTTCTC	63	2654
1100367	89	108	GGCATTGCTTATAACTTTCT	49	2655

Table 5

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	SEQ ID No: 4 Start Site	SEQ ID No: 4 Stop Site	Sequence (5' to 3')	ATXN3 (% control)	SEQ ID NO
1101399	291	310	TAAACCACTGAATAGAGAAA	91	2656
1101400	294	313	AGTTAAACCACTGAATAGAG	76	2657
1101401	295	314	AAGTTAAACCACTGAATAGA	107	2658
1101402	297	316	TCAAGTTAAACCACTGAATA	65	2659
1101403	298	317	TTCAAGTTAAACCACTGAAT	90	2660
1101404	300	319	AATTCAAGTTAAACCACTGA	89	2661

Table 6

Percent control of human ATXN3 RNA with 5-10-5 MOE gapmers with mixed internucleoside linkages

Compound Number	SEQ ID No: 5 Start Site	SEQ ID No: 5 Stop Site	Sequence (5' to 3')	ATXN3 (% control)	SEQ ID NO
1101448	9782	9801	CAAAGCAGTTAAATCTGGCC	96	2662
1101449	10192	10211	TGGGTTTATATATTTTTCTT	72	2663
1101449	10192	10211	TGGGTTTATATATTTTTCTT	100	2663
1101449	10192	10211	TGGGTTTATATATTTTTCTT	111	2663
1101450	10194	10213	TGTGGGTTTATATATTTTTC	78	2664
1101451	10235	10254	TAATCCAATGAATGCATCTC	79	2665
1101452	10588	10607	AAGTCACTGTTATATTAGTT	201	2666
1101453	10595	10614	GCATGTAAAGTCACTGTTAT	121	2667
1101454	10609	10628	AAAAAAAACCCATAGCATGT	109	2668
1101455	10610	10629	GAAAAAAAACCCATAGCATG	89	2669
1101456	10611	10630	AGAAAAAAAACCCATAGCAT	81	2670
1101457	10615	10634	GAGGAGAAAAAAAACCCATA	95	2671

1101458	10630	10649	ATTTCTTGAAGATGAGAGGA	99	2672
1101459	10683	10702	AGCAGATTCCTGACACTGTG	110	2673
1101460	10684	10703	GAGCAGATTCCTGACACTGT	118	2674
1101461	10697	10716	AATTATACAGAAAGAGCAGA	84	2675
1101462	10699	10718	ACAATTATACAGAAAGAGCA	127	2676
1101463	10701	10720	TAACAATTATACAGAAAGAG	95	2677
1101464	10702	10721	GTAACAATTATACAGAAAGA	99	2678
1101465	10703	10722	TGTAACAATTATACAGAAAG	109	2679
1101466	10704	10723	CTGTAACAATTATACAGAAA	124	2680
1101467	10705	10724	CCTGTAACAATTATACAGAA	71	2681
1101468	10706	10725	TCCTGTAACAATTATACAGA	90	2682
1101469	11124	11143	AGGATGAGATACAAGGTCAA	108	2683
1101470	11556	11575	ACATAAAGCCATTATGTCAG	91	2684
1101471	11557	11576	TACATAAAGCCATTATGTCA	96	2685
1101472	11558	11577	GTACATAAAGCCATTATGTC	74	2686
1101473	11564	11583	AGCCATGTACATAAAGCCAT	105	2687
1101474	12097	12116	AAAAACCACCTTGTAGCTAG	107	2688
1101475	12100	12119	AATAAAAACCACCTTGTAGC	86	2689
1101476	12101	12120	GAATAAAAACCACCTTGTAG	79	2690
1101477	12102	12121	AGAATAAAAACCACCTTGTA	77	2691
1101478	12103	12122	CAGAATAAAAACCACCTTGT	77	2692
1101479	12105	12124	CCCAGAATAAAAACCACCTT	72	2693
1101480	12106	12125	ACCCAGAATAAAAACCACCT	89	2694
1101481	12113	12132	CATGGCAACCCAGAATAAAA	88	2695
1101482	12114	12133	GCATGGCAACCCAGAATAAA	94	2696
1101483	12502	12521	CTGGAACACTTTTAAAAAAT	87	2697
1101484	12535	12554	TTTCTTACTCCCCTATGCCC	95	2698
1101485	12541	12560	TTCCACTTTCTTACTCCCCT	87	2699
1101485	12541	12560	TTCCACTTTCTTACTCCCCT	110	2699
1101485	12541	12560	TTCCACTTTCTTACTCCCCT	93	2699
1101486	12542	12561	TTTCCACTTTCTTACTCCCC	79	2700
1101487	12626	12645	ATGTGAATATCCTGCCTCCA	111	2701
1101488	12688	12707	ACCTTATTCAGCCAGAGTTG	92	2702
1101489	12691	12710	GCAACCTTATTCAGCCAGAG	79	2703
1101490	12725	12744	GCCCATACTTTCCAGGTGCC	77	2704
1101491	12727	12746	GAGCCCATACTTTCCAGGTG	102	2705
1101492	12732	12751	TACTGGAGCCCATACTTTCC	98	2706
1101493	12785	12804	CCCTTTACCACTTTTGTGCA	70	2707
1101494	12788	12807	CATCCCTTTACCACTTTTGT	81	2708
1101495	12827	12846	CATGACAGCCAAGATGCCAG	87	2709
1101496	12938	12957	TTAGCATTTCTCTTCTGTTG	78	2710
1101497	13356	13375	TGTTGCTTTCCTTTCCTGCA	97	2711
1101498	13395	13414	GATTTCAGTCTACATCTAAC	111	2712

1101499	13399	13418	TCCTGATTTCAGTCTACATC	88	2713
1101500	13402	13421	ACCTCCTGATTTCAGTCTAC	96	2714
1101501	13414	13433	AGTTTTAACCACACCTCCTG	91	2715
1101502	13418	13437	AAAGAGTTTTAACCACACCT	92	2716
1101503	13428	13447	AGCCTCTTTCAAAGAGTTTT	90	2717
1101504	13917	13936	TCTGAAATTAATAATGGTGT	117	2718
1101505	13919	13938	GCTCTGAAATTAATAATGGT	89	2719
1101506	13968	13987	GCCTTGTTTTCTTCCAAGAA	119	2720
1101507	14062	14081	ACAAAACATCAAGAATTCTA	92	2721
1101508	14064	14083	CAACAAAACATCAAGAATTC	101	2722
1101509	14065	14084	TCAACAAAACATCAAGAATT	125	2723
1101510	14066	14085	TTCAACAAAACATCAAGAAT	86	2724
1101511	14069	14088	GTTTTCAACAAAACATCAAG	143	2725
1101512	14070	14089	TGTTTTCAACAAAACATCAA	86	2726
1101513	14074	14093	CTTCTGTTTTCAACAAAACA	94	2727
1101514	14076	14095	TGCTTCTGTTTTCAACAAAA	90	2728
1101515	14111	14130	GAATCTTTCTAAAACTTACC	62	2729
1101516	14112	14131	AGAATCTTTCTAAAACTTAC	81	2730
1101517	14115	14134	TACAGAATCTTTCTAAAACT	80	2731
1101518	14207	14226	GTACCAAGATTATATTGCCT	90	2732
1101519	14208	14227	TGTACCAAGATTATATTGCC	84	2733
1101520	14209	14228	TTGTACCAAGATTATATTGC	102	2734
1101521	14212	14231	ATGTTGTACCAAGATTATAT	116	2735
1101521	14212	14231	ATGTTGTACCAAGATTATAT	70	2735
1101521	14212	14231	ATGTTGTACCAAGATTATAT	130	2735
1101522	14214	14233	AAATGTTGTACCAAGATTAT	76	2736
1101523	14239	14258	AAGTCTTATTCATTGCAGCT	80	2737
1101524	14240	14259	TAAGTCTTATTCATTGCAGC	95	2738
1101525	14430	14449	TCTGAATTTCTAAGCATTAG	99	2739
1101526	14431	14450	TTCTGAATTTCTAAGCATTA	95	2740
1101527	14432	14451	TTTCTGAATTTCTAAGCATT	98	2741
1101528	14456	14475	GACTTTAAAATTTAGTCTGA	83	2742
1101529	14459	14478	GTAGACTTTAAAATTTAGTC	78	2743
1101530	14460	14479	AGTAGACTTTAAAATTTAGT	92	2744
1101531	14461	14480	AAGTAGACTTTAAAATTTAG	81	2745
1101532	14507	14526	TCAAAATGAATTTATTTATG	91	2746
1101533	14509	14528	CATCAAAATGAATTTATTTA	87	2747
1101534	14515	14534	GAAAACCATCAAAATGAATT	120	2748
1101535	14518	14537	TGAGAAAACCATCAAAATGA	63	2749
1101536	14519	14538	CTGAGAAAACCATCAAAATG	102	2750
1101537	14520	14539	TCTGAGAAAACCATCAAAAT	114	2751
1101538	14523	14542	TGTTCTGAGAAAACCATCAA	150	2752
1101539	14850	14869	TTTCCATTACTCAAGCAGTG	74	2753

1101540	15114	15133	AAAGACATACAAGTTTGATA	127	2754
1101541	15119	15138	AGTTAAAAGACATACAAGTT	83	2755
1101542	15120	15139	AAGTTAAAAGACATACAAGT	104	2756
1101543	15189	15208	TGGTGGGTACATAAGGTTCA	105	2757
1101544	15215	15234	AGGAACTGATAATTGTTGAA	86	2758
1101545	15232	15251	GTGAAACAAGAATTGTCAGG	91	2759
1101546	15333	15352	GCTTCAAAATAATGGAAGTT	107	2760
1101547	15334	15353	TGCTTCAAAATAATGGAAGT	107	2761
1101548	15335	15354	GTGCTTCAAAATAATGGAAG	106	2762
1101549	15336	15355	TGTGCTTCAAAATAATGGAA	90	2763
1101550	15337	15356	ATGTGCTTCAAAATAATGGA	75	2764
1101551	15379	15398	CTTAATAAATAATGTGATAA	94	2765
1101552	15381	15400	AACTTAATAAATAATGTGAT	100	2766
1101553	15382	15401	AAACTTAATAAATAATGTGA	124	2767
1101554	15441	15460	CTATGTCCTAAAAGTTTCTC	77	2768
1101555	15442	15461	GCTATGTCCTAAAAGTTTCT	136	2769
1101556	15455	15474	AATTAACATAAAAGCTATGT	84	2770
1101557	15457	15476	GTAATTAACATAAAAGCTAT	96	2771
1101557	15457	15476	GTAATTAACATAAAAGCTAT	79	2771
1101557	15457	15476	GTAATTAACATAAAAGCTAT	114	2771
1101558	15459	15478	AAGTAATTAACATAAAAGCT	86	2772
1101559	15472	15491	TAGTGCAGAAATTAAGTAAT	98	2773
1101560	15479	15498	GGATGGCTAGTGCAGAAATT	104	2774
1101561	15507	15526	CTAGTGCAGAAAATTAGAAG	96	2775
1101562	15513	15532	GGATAGCTAGTGCAGAAAAT	88	2776
1101563	15619	15638	AGAATGAGACATGTAAGTAT	107	2777
1101564	15627	15646	GGTGAAAAAGAATGAGACAT	69	2778
1101565	15631	15650	CCTGGGTGAAAAAGAATGAG	70	2779
1101566	15633	15652	CACCTGGGTGAAAAAGAATG	106	2780
1101567	16440	16459	AACAAAAATTATCTAGATCC	94	2781
1101568	16913	16932	GTTGAGTTTTTATATTTGAT	69	2782
1101569	16915	16934	GGGTTGAGTTTTTATATTTG	90	2783
1101570	19195	19214	AAGATACTACTATAGCATAG	88	2784
1101571	19196	19215	GAAGATACTACTATAGCATA	78	2785
1101572	19197	19216	GGAAGATACTACTATAGCAT	107	2786
1101573	19198	19217	TGGAAGATACTACTATAGCA	84	2787

Example 2: Effect of 5-10-5 MOE gapmers with mixed internucleoside linkages on human ATXN3 *in vitro*, multiple doses

Modified oligonucleotides selected from the examples above were tested at various doses in A431 cells by free uptake. Compound No. 650528, described in WO 2018/089805, was also tested. Compound No. 650528 is a 5-8-5 MOE gapmer, having a sequence (from 5' to 3') GCATCTTTTCATACTGGC (incorporated herein as SEQ ID NO: 2788), wherein each cytosine is a 5-methyl cytosine, each internucleoside linkage is either a phosphodiester

internucleoside linkage or a phosphorothioate internucleoside linkage and the internucleoside linkage motif is sooossssssssooss, where 's' represents a phosphorothioate internucleoside linkage and 'o' represents a phosphodiester internucleoside linkage, and each of nucleosides 1-5 and 14-18 comprise a 2'-O-methyoxyethyl group.

Cells were plated at a density of 10,000 cells per well with 109.4 nM, 437.5 nM, 1,750.0 nM, and 7,000.0 nM concentrations of modified oligonucleotide, as specified in the tables below. After a treatment period of approximately 48 hours, total RNA was isolated from the cells and ATXN3 RNA levels were measured by RT-qPCR. Human ATXN3 primer probe set RTS38920 (described hereinabove in Example 1) was used to measure RNA levels. ATXN3 RNA levels were adjusted according to total RNA content, as measured by RiboGreen®. Results are presented in the table below as percent ATXN3 RNA levels relative to untreated control cells. As illustrated in the table below, ATXN3 RNA levels were reduced in a dose-dependent manner in modified oligonucleotide-treated cells. IC_{50} was calculated using the "log(inhibitor) vs. response – variable slope (4 parameters)" formula using Prism6 software.

Table 7

Dose-dependent reduction of human ATXN3 RNA by modified oligonucleotides

Compound Number	ATXN3 level (% control)				IC_{50} (μM)
	109.4 nM	437.5 nM	1,750.0 nM	7,000.0 nM	
650528	100	57	39	30	1.3
1100379	77	66	37	23	0.9
1100384	86	64	35	25	1.0
1100397	68	49	25	15	0.4
1100398	63	46	26	14	0.3
1100399	81	39	39	22	0.6
1100403	61	48	32	20	0.3
1100405	60	41	25	16	0.2
1100406	85	45	24	12	0.5
1100407	56	27	15	8	0.1
1100408	61	45	21	13	0.3
1100409	56	34	19	12	0.1
1100410	69	64	38	27	0.8
1100429	89	65	38	24	1.1
1100430	90	72	53	30	1.9
1100434	77	51	30	18	0.6
1100468	72	61	44	36	1.3
1100475	68	52	28	21	0.5
1100479	89	89	56	34	2.9
1100557	77	63	47	36	1.5
1100559	76	53	29	18	0.6
1100560	56	45	27	20	0.2
1100566	64	34	13	7	0.2
1100567	68	50	31	22	0.5
1100568	97	71	41	30	1.6
1100571	97	79	38	25	1.5

1100572	79	74	45	30	1.5
1100574	78	68	46	24	1.2
1100580	102	74	43	27	1.6
1100583	54	46	26	12	0.2
1100584	61	42	23	10	0.2
1100585	67	48	25	15	0.4
1100589	74	53	32	20	0.6
1100590	78	39	17	6	0.4
1100591	71	46	26	16	0.4
1100592	82	86	56	57	> 7.0
1100597	73	47	26	18	0.4
1100641	121	95	78	66	> 7.0
1100666	71	48	31	20	0.5
1100667	80	53	38	25	0.8
1100668	78	62	39	26	1.0
1100669	75	41	23	14	0.4
1100673	55	25	15	10	< 0.1
1100697	59	49	27	20	0.3
1100719	72	60	28	15	0.6
1100725	53	30	17	10	< 0.1
1100729	86	70	44	38	1.9
1100730	58	41	25	16	0.2
1100732	62	43	23	22	0.3
1100753	60	52	33	30	0.4
1100756	60	48	35	29	0.3
1100768	76	52	32	19	0.6
1100788	88	72	48	30	1.7
1100789	90	67	56	40	2.8
1100796	63	48	37	26	0.4
1100802	50	34	23	19	< 0.1
1100809	56	44	21	19	0.2
1100810	65	41	20	14	0.3
1100839	63	36	14	8	0.2
1100846	104	78	54	29	2.2
1100863	44	31	19	15	< 0.1
1100864	67	35	19	16	0.2
1100865	56	34	18	13	0.1
1100872	65	40	23	13	0.3
1100873	46	36	18	12	< 0.1
1100897	74	50	38	33	0.8
1100898	72	57	36	31	0.8
1100899	68	52	30	24	0.5
1100900	58	41	28	23	0.2

1100901	43	32	21	17	< 0.1
1100902	58	35	24	19	0.2
1100903	72	53	32	24	0.6
1100906	56	42	26	16	0.2
1100907	26	26	15	12	< 0.1
1100910	55	40	26	19	0.2
1100911	75	48	30	18	0.5
1100914	27	12	7	5	< 0.1
1100914	26	11	6	5	< 0.1
1100914	26	12	7	7	< 0.1
1100914	29	11	6	5	< 0.1
1100914	38	16	8	5	< 0.1
1100914	34	13	7	5	< 0.1
1100914	28	13	7	5	< 0.1
1100914	27	13	6	5	< 0.1
1100914	33	14	7	5	< 0.1
1100914	33	12	6	6	< 0.1
1100914	30	13	8	6	< 0.1
1100914	28	15	8	6	< 0.1
1100915	51	23	11	6	< 0.1
1100916	35	22	14	12	< 0.1
1100917	48	29	14	10	< 0.1
1100920	46	30	15	9	< 0.1
1100921	70	54	32	20	0.5
1100924	57	34	25	19	0.1
1100925	76	52	33	23	0.6
1100928	39	28	17	14	< 0.1
1100980	51	39	25	16	0.1
1100988	62	41	27	22	0.3
1100989	64	38	22	14	0.2
1100990	36	25	13	12	< 0.1
1100991	55	35	17	13	0.1
1100992	69	49	36	29	0.6
1100995	80	74	46	37	1.9
1100996	60	44	28	18	0.3
1100997	66	40	26	16	0.3
1100998	79	68	41	28	1.2
1100999	70	58	40	34	0.9
1101000	61	39	22	18	0.2
1101001	53	43	25	22	0.2
1101004	73	57	63	41	3.3
1101049	69	47	30	24	0.4
1101053	82	39	22	16	0.4

1101054	62	47	26	21	0.3
1101057	72	57	34	26	0.7
1101058	94	65	44	20	1.2
1101065	60	34	24	20	0.2
1101066	69	47	30	22	0.4
1101099	55	33	21	16	0.1
1101101	40	23	13	12	< 0.1
1101120	66	50	37	30	0.5
1101121	71	54	36	20	0.6
1101122	77	48	33	25	0.6
1101201	60	54	36	34	0.5
1101202	35	21	15	13	< 0.1
1101203	56	40	32	30	0.2
1101204	53	42	30	28	0.1
1101339	77	60	34	24	0.8
1101349	54	42	19	11	0.2
1101350	63	43	33	18	0.3
1101351	79	58	33	24	0.8
1101352	97	55	26	13	0.8
1101364	76	53	35	24	0.7
1101383	62	46	36	27	0.4
1101384	57	44	30	19	0.2
1101411	63	26	22	18	0.1
1101600	72	42	28	15	0.4
1101607	84	66	50	40	2.2
1101657	82	55	28	20	0.7
1101659	88	59	35	20	0.9
1101682	78	58	45	28	1.1
1101689	91	61	54	44	2.9
1101817	111	106	64	38	4.3
1101873	65	49	38	35	0.6
1101918	81	77	40	32	1.6
1101920	52	41	23	11	0.1
1101974	26	7	4	4	< 0.1
1101975	32	15	7	5	< 0.1
1102024	63	44	21	10	0.3
1102028	41	20	9	6	< 0.1
1102049	61	45	30	19	0.3
1102050	61	27	13	8	0.1
1102052	63	51	32	26	0.4
1102074	41	21	12	6	< 0.1
1102077	73	61	37	25	0.8
1102084	59	41	21	18	0.2

1102085	55	43	19	15	0.2
1102090	69	44	27	20	0.4
1102103	83	54	34	19	0.7
1102104	55	28	10	8	< 0.1
1102108	79	67	45	21	1.1
1102110	87	48	26	14	0.6
1102119	109	109	76	60	> 7.0
1102128	77	58	30	16	0.6
1102129	83	58	37	28	1.0
1102130	58	38	20	13	0.2
1102131	73	57	30	16	0.6
1102134	84	73	55	34	2.3
1102180	82	55	42	32	1.1
1102195	83	73	49	36	2.1
1102198	60	41	26	15	0.2
1102200	95	69	47	27	1.6
1102202	91	56	32	19	0.8
1102239	78	64	42	33	1.3
1102262	88	71	48	34	1.9
1102328	60	50	33	21	0.3
1102329	65	37	22	11	0.2
1102336	58	34	20	13	0.2
1102351	66	53	29	28	0.5
1102353	69	50	23	11	0.4
1102374	78	67	53	36	2.0
1102379	67	59	32	21	0.6
1102385	69	38	20	15	0.3
1102424	79	72	46	27	1.4
1102541	63	50	26	17	0.3
1102547	94	78	59	51	> 7.0
1102551	87	50	23	11	0.6
1102552	67	51	30	28	0.5
1102557	74	35	21	10	0.3
1102562	73	60	35	20	0.7
1102563	64	49	36	22	0.4
1102573	82	46	26	18	0.6
1102574	61	43	24	17	0.2
1102579	62	59	32	22	0.5
1102580	67	46	26	16	0.4
1102598	93	54	26	14	0.7
1102599	66	47	23	11	0.3
1102600	77	56	35	22	0.7
1102612	71	51	35	24	0.6

1102637	92	63	37	21	1.1
1102646	75	56	35	30	0.8
1102655	82	83	55	38	3.1
1102657	71	39	18	12	0.3
1102663	63	55	38	27	0.5
1102666	58	30	15	9	0.1
1102667	73	50	26	15	0.5
1102668	88	64	44	32	1.5
1102669	67	68	48	32	1.4
1102677	68	49	27	20	0.4
1102678	65	35	25	17	0.2
1102679	72	58	48	36	1.3
1102683	55	45	31	17	0.2
1102684	82	44	20	12	0.5
1102690	68	60	36	33	0.8
1102695	90	53	27	18	0.7
1102722	67	39	20	9	0.3
1102723	71	48	28	21	0.5
1102725	48	37	23	10	< 0.1
1102726	88	56	40	25	1.0
1102734	81	57	31	19	0.7
1102750	69	61	35	23	0.7
1102759	69	51	26	24	0.4
1102760	73	70	59	47	5.5
1102789	76	65	38	23	0.9
1102794	55	29	13	8	< 0.1
1102801	80	56	36	29	0.9
1102802	77	56	28	23	0.6
1102811	29	16	8	6	< 0.1
1102841	64	39	29	23	0.3

Example 3: Tolerability of modified oligonucleotides complementary to human ATXN3 in wild-type mice

Modified oligonucleotides described above were tested in wild-type female C57/Bl6 mice to assess the tolerability of the oligonucleotides. Wild-type female C57/Bl6 mice each received a single ICV dose of 700µg of modified oligonucleotide listed in the table below. Each treatment group consisted of 2 mice. A group of 2 mice received PBS as a negative control. At 3 hours post-injection, mice were evaluated according to 7 different criteria. The criteria are (1) the mouse was bright, alert, and responsive; (2) the mouse was standing or hunched without stimuli; (3) the mouse showed any movement without stimuli; (4) the mouse demonstrated forward movement after it was lifted; (5) the mouse demonstrated any movement after it was lifted; (6) the mouse responded to tail pinching; (7) regular breathing. For each of the 7 criteria, a mouse was given a subscore of 0 if it met the criteria and 1 if it did not (the functional observational battery score or FOB score). After all 7 criteria were evaluated, the scores were summed for each mouse and averaged within each treatment group. The results are presented in the table below.

Table 8

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100397	0.00
1100405	0.00
1100406	0.00
1100407	1.00
1100528	1.00
1100534	2.00
1100535	2.00
1100540	3.50
1100542	1.50
1100566	3.00
1100585	0.00
1100590	2.00
1100725	3.00
1100873	0.00
1100914	4.50
1100915	5.00
1100920	0.00
1100990	6.50
1100991	5.00
1101101	3.50
1101339	6.00
1101351	1.00
1101974	0.00
1101975	0.00
1102024	0.00
1102028	0.00
1102050	6.50
1102130	0.00
1102131	0.00
1102336	0.00
1102353	0.00
1102551	5.00
1102557	5.50
1102574	0.00
1102580	0.00
1102599	0.00
1102657	0.00
1102811	0.50
1102970	0.00
1102977	0.00
1102978	0.00

1102979	0.00
1103103	2.00

Table 9

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100379	0.00
1100398	1.00
1100399	3.00
1100409	4.00
1100521	4.00
1100527	1.00
1100536	3.00
1100541	4.00
1100544	4.00
1100571	3.00
1100572	2.00
1100667	5.50
1100673	1.00
1100730	3.00
1100732	3.00
1100809	1.00
1100864	2.00
1100865	1.00
1100907	4.00
1100911	1.00
1100980	4.00
1101054	2.00
1101065	4.00
1101121	3.00
1101122	2.00
1101350	3.00
1101352	3.00
1101411	1.00
1101657	1.00
1102084	2.00
1102090	3.00
1102128	3.00
1102198	1.00
1102562	3.00
1102563	3.00
1102612	3.00
1102667	1.00
1102677	3.00

1102683	1.00
1102684	1.00
1102725	2.50
1102980	1.00
1103001	3.00
1103014	1.00
1103069	2.00

Example 4: Activity of modified oligonucleotides complementary to human ATXN3 in transgenic mice

Modified oligonucleotides described above were tested in the ATXN3 YAC transgenic mouse model which contains the full-length human ATXN3 disease gene harboring an expanded CAG repeat (CAG_{84}, Q84). The hemizygous SCA3-Q84.2 mice are designated as wt/Q84 and were described in Costa Mdo C., et al., *Toward RNAi Therapy for the Polyglutamine Disease Machado–Joseph Disease.* Mol Ther, 2013. 21 (10): 1898-908." Compound No. 650528, described hereinabove and in WO 2018/089805, was also tested

The ATXN3 transgenic mice were divided into groups of 3 mice each. Mice in each group were given a single ICV bolus of oligonucleotide at a dose of 300 µg and sacrificed two weeks later. A group of 4-6 mice was injected with PBS and served as the control group to which oligonucleotide-treated groups were compared. After two weeks, mice were sacrificed and RNA was extracted from brain tissue for real-time PCR analysis of measurement of RNA expression of ATXN3 using primer probe set RTS39540 (forward sequence CCTTCTTCCTGCGCCTTATT, designated herein as SEQ ID NO: 12; reverse sequence TCATGGTGGGTACGTATGTTTAG, designated herein as SEQ ID NO: 13; probe sequence AGTATGCAGGCAAGTCTCCTTCTGT, designated herein as SEQ ID NO: 14). Results are presented as percent change of RNA, relative to PBS control, normalized with cyclophilin A. As shown in the tables below, human ATXN3 RNA was reduced in various tissues.

Table 10

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	29	43	76	30
1100914	17	24	68	16
1100873	48	82	71	57
1100585	56	77	70	54
1100590	21	34	54	73
1102130	33	54	63	22
1102977	45	61	78	33
1102353	33	48	69	57
1102599	28	54	57	42
1102979	34	53	87	34
1102978	60	76	76	37
1101920	55	79	70	68
1100572	56	87	70	70
1100571	33	55	55	79
1100667	59	86	100	39

Table 11

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	25	42	71	29
1100914	15	19	56	17
1100528	71	67	80	68
1100915	27	27	46	27
1100397	49	58	60	52
1100406	55	58	69	51
1102050	41	46	67	37
1102024	47	41	72	51
1101101	31	37	71	34
1102551	56	62	76	61
1102574	29	40	60	30
1102970	64	60	85	68
1102336	53	42	68	58
1102811	16	22	40	17
1102028	25	25	59	23
1100434	78	75	84	78
1100559	53	41	76	50
1101121	40	46	61	37
1100992	45	49	56	41
1100468	58	59	74	53
1100544	81	62	88	73
1100810	57	95	65	47
1100379	55	54	66	52
1100673	9	12	67	11
1102669	72	69	81	70
1102725	50	49	76	50
1103014	50	52	70	40
1102667	55	111	72	58

Table 12

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	24	43	80	31
1100914	14	18	59	15
1100429	69	72	80	80
1100542	78	78	84	73
1100991	26	51	71	53
1100725	18	27	67	22
1102084	46	72	88	55
1101351	66	87	92	65
1102131	35	36	76	37
1103103	28	42	75	36
1102557	58	79	87	74
1102657	12	19	59	17
1100839	25	40	54	35

1100864	41	68	67	54
1100907	32	49	63	41

Table 13

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	24	37	93	31
1100914	14	22	68	19
1102108	61	54	88	63
1100697	44	48	75	39
1100902	38	45	83	39
1101383	52	65	101	65
1100900	46	62	92	56
1102562	45	54	64	55
1102637	30	29	50	34
1101203	52	65	70	68
1102612	33	47	73	39
1102198	51	75	96	66

Table 14

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	28	48	69	31
1100914	20	17	52	16
1102677	83	95	88	86
1102998	41	51	82	47
1103069	25	39	67	29
1100753	39	48	51	37

Table 15

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	23	38	74	30
1100914	13	15	50	18
1100920	76	86	104	84
1101352	68	84	93	69
1101099	54	68	101	62
1100990	15	41	60	22
1100872	53	65	81	62
1101122	30	23	61	31
1100898	34	37	84	34
1101918	69	93	71	71
1100405	49	58	98	45
1102580	56	79	85	49
1100407	50	63	91	50

1101054	29	31	75	36
1101350	56	74	78	64
1101975	31	58	70	38
1100921	64	86	83	65

Table 16

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	25	54	58	26
1100914	13	13	39	15
1100865	37	37	60	36
1100730	19	26	34	20
1100584	47	45	51	45
1101120	49	65	67	47
1100911	36	52	54	38
1102090	38	50	71	36
1102128	34	41	56	31
1100541	57	72	74	68
1100809	40	48	69	37
1102541	51	75	56	56
1102666	34	52	58	31
1100398	60	64	65	64
1100399	46	49	59	47
1100410	52	69	70	48
1100732	55	80	72	58

Table 17

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	21	38	67	26
1100914	14	18	43	16
1100557	53	78	78	74
1100980	23	45	80	24
1102600	48	55	86	44
1102980	41	43	67	43
1101657	17	23	57	19
1102684	65	85	110	73
1101202	28	33	66	27
1101659	29	39	77	27
1102103	36	43	81	41
1101873	41	49	80	41
1102202	69	78	98	70
1102180	68	72	106	75
1102239	63	68	92	82
1102678	73	79	92	77
1102052	68	83	100	72

Table 18

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
PBS	100	100	100	100
650528	28	35	83	27
1100914	13	11	46	12
1102129	28	26	56	20
1101053	42	56	97	43
1100430	81	75	76	78
1100666	50	44	70	47
1100756	45	64	71	42
1102598	33	31	56	30
1100863	52	53	77	52
1102646	63	80	87	62
1102750	59	66	70	57
1100802	29	36	61	36
1100906	44	46	69	52
1102379	64	69	94	72
1102663	60	83	63	69
1102679	80	93	92	92

Example 5: Tolerability of modified oligonucleotides complementary to human ATXN3 in wild-type mice

Modified oligonucleotides described above were tested in wild-type female C57/Bl6 mice to assess the tolerability of the oligonucleotides. Wild-type female C57/Bl6 mice each received a single ICV dose of 700µg of modified oligonucleotide listed in the table below. Each treatment group consisted of 4 mice. A group of 3-4 mice received PBS as a negative control. Also tested in several studies were comparator Compound No. 650528, a 5-8-5 MOE gapmer with mixed PO/PS internucleoside linkages complementary to human ATXN3 described hereinabove and in WO 2018/089805 and the following LNA comparator compounds: Compound No. 1244463 (a 3-9-3 LNA gapmer with uniform PS internucleoside linkages complementary to human ATXN3); Compound No. 1244464 (a 3-10-3 LNA gapmer with uniform PS internucleoside linkages complementary to human ATXN3); Compound No. 1244465 (a 3-10-3 LNA gapmer with uniform PS internucleoside linkages complementary to human ATXN3); Compound No. 1244466 (a 3-9-3 LNA gapmer with uniform PS internucleoside linkages complementary to human ATXN3); and Compound No. 1244467 (a 2-9-3 LNA gapmer with uniform PS internucleoside linkages complementary to human ATXN3), described in WO2013/138353 were tested.

At 3 hours post-injection, mice were evaluated according to 7 different criteria. The criteria are (1) the mouse was bright, alert, and responsive; (2) the mouse was standing or hunched without stimuli; (3) the mouse showed any movement without stimuli; (4) the mouse demonstrated forward movement after it was lifted; (5) the mouse demonstrated any movement after it was lifted; (6) the mouse responded to tail pinching; (7) regular breathing. For each of the 7 criteria, a mouse was given a subscore of 0 if it met the criteria and 1 if it did not (the functional observational battery score or FOB score). After all 7 criteria were evaluated, the scores were summed for each mouse and averaged within each treatment group. The results are presented in the table below.

Table 19

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
650528	0.00
1100559	4.00
1100802	5.75
1100839	4.25
1100898	0.00
1100914	5.25
1101202	5.25
1101659	1.50
1102129	2.75
1102598	0.00
1102637	3.50

Table 20

FOB scores in wild-type mice

Compound Number	3 hour FOB
650528	0.00
1100408	6.25
1100673	0.00
1100725	4.50
1100730	2.75
1100914	4.00
1100917	6.00
1101000	4.75
1101122	3.25
1101657	0.00
1102130	0.00
1102131	0.75
1102574	1.00
1102811	2.25

Table 21

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100369	0.25
1100479	3.25
1100505	5.00
1100508	6.00
1101375	0.00
1101721	5.00
1101853	0.00
1102690*	0.00
1102706	1.00
1102808	1.75
1103041	3.00

Table 22

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1101736	0.00

Table 23

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100505	4.00
1100506	1.50
1100672	0.00
1100731	1.25
1102811	2.25
1103041	3.25

Table 24

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100723	0.00
1100724	1.00
1100728	0.75
1100729	0.50

Table 25

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1100506	2.00
1100731	3.75

Table 26

FOB scores in wild-type mice

Compound Number	3 hour FOB
PBS	0.00
1244463	7.00
1244464	7.00
1244465	7.00
1244466	7.00
1244467	7.00

Example 6: Activity of modified oligonucleotides complementary to human ATXN3 RNA in transgenic mice

Modified oligonucleotides were tested in the ATXN3 YAC transgenic mouse model which contains the full-length human ATXN3 disease gene harboring an expanded CAG repeat (CAG_{84}, Q84). The hemizygous SCA3-Q84.2 mice are designated as wt/Q84 and were described in Costa Mdo C., et al., *Toward RNAi Therapy for the Polyglutamine Disease Machado–Joseph Disease.* Mol Ther, 2013. 21 (10): 1898-908.

The ATXN3 transgenic mice were divided into groups of 2-3 mice each. Mice in each group were given a single ICV bolus of oligonucleotide at a dose of 300 μg and sacrificed two weeks later. A group of 2 to 5 mice was injected with PBS and served as the control group to which oligonucleotide-treated groups were compared. After two weeks, mice were sacrificed, and RNA was extracted from various regions of the central nervous system. ATXN3 RNA

levels were measured by quantitative real-time RTPCR using human primer probe set RTS43981 (forward sequence TGACACAGACATCAGGTACAAATC, designated herein as SEQ ID NO: 2798; reverse sequence TGCTGCTGTTGCTGCTT, designated herein as SEQ ID NO: 2799; probe sequence AGCTTCGGAAGAGACGAGAAGCCTA, designated herein as SEQ ID NO: 2800). Results are presented as percent change of RNA, relative to PBS control, normalized to mouse cyclophilin A measured using mouse primer probe set m_cyclo24 (forward sequence TCGCCGCTTGCTGCA, designated herein as SEQ ID NO: 2801; reverse sequence ATCGGCCGTGATGTCGA, designated herein as SEQ ID NO: 2802; probe sequence CCATGGTCAACCCCACCGTGTTC, designated herein as SEQ ID NO: 2803). Also tested in several studies was comparator Compound No. 650528, a 5-8-5 MOE gapmer with mixed PO/PS internucleoside linkages complementary to human ATXN3 described hereinabove and in WO 2018/089805. As shown in the tables below, human ATXN3 RNA was reduced in various tissues.

Table 27

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	38	41	79	40
1100408	28	40	68	32
1100409	30	55	59	36
1100521	68	87	83	74
1100527	76	83	79	82
1100534	57	71	97	59
1100535	77	96	100	84
1100536	76	103	80	90
1100540	67	69	89	68
1100566	68	94	85	74
1100673	17	14	53	16
1100914	23	17	50	24
1101000	34	37	69	34
1101065	43	62	66	42
1101339	51	56	78	57
1101411	29	52	56	30
1101974	17	22	50	19
1102329	46	48	73	49
1102563	42	45	78	41
1102657	20	18	52	19
1102683	27	29	60	27
1102811	27	38	66	23
1103001	45	53	71	52

Table 28

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	30	42	67	34
1100670	61	75	72	54
1100671	60	70	73	45
1100674	64	74	84	58
1100910	34	43	62	37
1100912	55	52	71	53
1100917	38	32	68	35

Table 29

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	39	61	81	38
1100505	32	38	64	34
1100522	59	85	89	64
1100523	88	103	83	96
1100597	63	85	85	71
1100914	22	29	63	28
1101349	45	70	71	52
1101370	67	107	97	71
1101600	41	47	70	44
1102328	39	57	66	37
1102794	51	71	86	62
1102939	63	63	87	76
1102941	50	80	84	60
1103073	44	73	68	51
1103116	44	63	78	47

Table 30

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	32	48	74	34

1100369	22	40	54	30
1100382	64	78	66	53
1100384	56	94	67	53
1100454	44	72	49	45
1101388	58	53	74	48
1101601	56	62	62	58
1101615	81	108	85	82
1101721	21	46	61	29
1101755	53	82	59	60
1101926	67	87	71	63
1101992	93	89	78	79
1102043	71	86	69	60
1102062	45	70	66	55
1102147	58	55	56	48
1102166	72	85	69	56
1102216	39	52	60	42
1102322	71	88	67	62
1102361	66	106	75	80
1102424	52	72	68	61
1102692	62	59	64	54
1102793	64	107	76	81
1103067	61	104	75	86
1103077	64	82	74	66
1103084	37	60	69	53

Table 31

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	49	30	90	43
1100479	57	34	71	47
1101375	59	45	74	48
1101609	86	84	104	83
1101667	84	68	100	82
1101764	85	68	93	72
1101853	65	45	78	53
1101962	79	59	92	67
1102195	111	65	98	73
1102426	76	61	79	69
1102690	53	33	80	42
1102787	78	65	106	87
1102808	65	47	88	58
1102865	92	72	101	81
1102957	75	58	81	71

1102981	76	56	94	66
1102997	85	62	97	74
1103105	68	49	85	56

Table 32

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	38	43	84	42
1100514	70	79	87	81
1101616	48	50	75	57
1101683	71	83	90	88
1101689	61	73	85	71
1101786	87	101	113	99
1101811	66	90	90	73
1101817	88	73	98	96
1101828	89	102	97	104
1102097	75	90	100	83
1102144	58	73	86	74
1102162	71	79	90	81
1102220	57	54	84	59
1102228	78	102	108	103
1102283	52	57	84	63
1102335	69	91	100	73
1102589	86	95	101	93
1102648	73	83	84	82
1102706	39	36	69	38
1102746	61	64	94	69
1102757	40	62	74	49
1102761	47	60	73	58
1102792	68	80	92	79
1102876	46	50	81	55
1102974	102	106	109	104

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Table 33

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	32	42	77	39
1100475	46	51	78	37
1100508	33	28	30	29
1101718	45	40	71	49

1101808	76	87	78	78
1101821	73	75	79	68
1101912	67	74	87	53
1101927	77	80	75	75
1101958	72	66	68	44
1102073	61	68	69	63
1102074	42	47	72	42
1102110	80	88	87	78
1102385	42	58	75	40
1102555*	86	85	79	64
1102722	78	91	80	75
1102734	43	69	77	50
1102789	65	73	82	59
1102848	76	92	96	84
1102953	80	82	81	78
1103012	80	90	79	70
1103041	34	23	61	35

* Group has only 1 animal

Table 34

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	36	47	81	44
1101736	33	32	61	38
1102060	57	53	82	56†
1102106	50	64	78	62
1102134	94	94	98	100
1102334	77	66	85	71
1102374	61	69	104	66
1102567	68	67	81	66
1102695	52	71	88	63
1102758	59	52	78	55
1102779	39	50	86	48
1102805	70	71	84†	75
1102898	63	71	73†	70
1103000	71	82	100	77
1103006	72	63	85	72
1103072	75	73	86	66

†Average of 2 PCR points

Table 35

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	28	43	76	32
1101974	13	10	48	15
1102130	21	29	73	23
1102132	86	70	91	70
1102133	85	86	101	85

Table 36

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	Cortex	Cerebellum	Brain Stem
650528	40	33	78	44
1101657	28	22	66	32
1102028	33	28	63	30
1102637	40	27	69	42
1102638	39	29	95	43
1102639	34	31	121	37
1102640	56	58	75	57
1102642	67	64	87	65

Table 37

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	caudal cortex	Cerebellum	Brain Stem
650528	28	49	68	40
1100723	40†	60	62	53
1100724	45	43	69	52
1100725	28	39	60	34
1100726	57	79	67	60
1100727	58	51	80	57
1100728	38	45	67	50
1100729	37	39	63	48
1102683	31	23	55	27

†Average of 2 PCR points

Table 38

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	caudal cortex	Cerebellum	Brain Stem
650528	38	39	80	31
1102574	32	41	70	34
1102595	102	94	98†	72
1102596	103	91	97	92
1102597	89	94	96	78
1102598	39	28	62	35
1102599	40	54	78	34
1102600	37	53	75	33
1102601	50	58	80	43
1102602	70	73	95	60
1102603	94	101	97	84
1102604	108	101	108	80
1102605	102	103	106	82

†Average of 2 PCR points

Table 39

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	hATXN3 Expression (% control)			
	Spinal cord	caudal cortex	Cerebellum	Brain Stem
650528	39	46	39	54†
1100505	46	55	41	49
1100506	57	60	37	62
1100672	37	36	46	32
1100731	35	33	32	33
1102811	19	24	29	23
1103041	36	26	37	29

†Average of 2 PCR points

Example 7: Effect of 5-10-5 MOE gapmers with mixed internucleoside linkages on human ATXN3 *in vitro*, multiple doses

Modified oligonucleotides selected from the examples above were tested at various doses in A431 cells by free uptake. Also tested was comparator Compound No. 650528, a 5-8-5 MOE gapmer with mixed PO/PS internucleoside linkages complementary to human ATXN3, described hereinabove and in WO 2018/089805.

Cells were plated at a density of 10,000 cells per well, and treated with 109.4 nM, 437.5 nM, 1,750.0 nM, and 7,000.0 nM concentrations of modified oligonucleotide, as specified in the tables below. After a treatment period of approximately 48 hours, total RNA was isolated from the cells and ATXN3 RNA levels were measured by RT-qPCR.

Human ATXN3 primer probe set RTS38920 (described hereinabove in Example 1) was used to measure RNA levels. ATXN3 RNA levels were adjusted according to total RNA content, as measured by RiboGreen®. In addition, ATXN3 RNA levels were also normalized to human GAPDH levels measured by human GAPDH primer-probe set RTS104 (forward sequence GAAGGTGAAGGTCGGAGTC, designated herein as SEQ ID NO: 2804; reverse sequence GAAGATGGTGATGGGATTTC, designated herein as SEQ ID NO: 2805; probe sequence CAAGCTTCCCGTTCTCAGCC, designated herein as SEQ ID: 2806). Results are presented in the table below as percent ATXN3 RNA levels relative to untreated control cells. IC_{50} was calculated using the "log(inhibitor) vs. normalized response – variable slope" formula using Prism7.01 software. In some cases, an IC_{50} could not be reliably calculated and the data point is marked as "N.C.".

Table 40

Dose-dependent reduction of human ATXN3 RNA by modified oligonucleotides

Compound Number	ATXN3 level (% control) normalized to ribogreen				IC_{50} (µM)
	109.4 nM	437.5 nM	1,750.0 nM	7000.0 nM	
650528	84	67	48	38	2.03
1100673	50	21	11	9	0.10
1100914	26	12	7	5	<0.10
1101657	93	53	31	17	0.69
1102130	85	46	24	13	0.47

Example 8: Tolerability of modified oligonucleotides complementary to human ATXN3 in rats, 3 mg dose

Modified oligonucleotides described above were tested in rats to assess the tolerability of the oligonucleotides. Sprague Dawley rats each received a single intrathecal (IT) dose of 3 mg of oligonucleotide listed in the table below. Each treatment group consisted of 4 rats. A group of four rats received PBS as a negative control. At 3 hours post-injection, movement in 7 different parts of the body were evaluated for each rat. The 7 body parts are (1) the rat's tail; (2) the rat's posterior posture; (3) the rat's hind limbs; (4) the rat's hind paws; (5) the rat's forepaws; (6) the rat's anterior posture; (7) the rat's head. For each of the 7 different body parts, each rat was given a sub-score of 0 if the body part was moving or 1 if the body part was paralyzed. After each of the 7 body parts were evaluated, the sub-scores were summed for each rat and then averaged for each group. For example, if a rat's tail, head, and all other evaluated body parts were moving 3 hours after the 3 mg IT dose, it would get a summed score of 0. If another rat was not moving its tail 3 hours after the 3 mg IT dose but all other evaluated body parts were moving, it would receive a score of 1. Results are presented as the average score for each treatment group. A comparator compound, 650528, a 5-8-5 MOE gapmer with mixed PO/PS internucleoside linkages complementary to human ATXN3 described hereinabove and in WO 2018/089805 was also tested.

Table 41

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100397	1.50
1100405	1.50
1100406	1.25
1100407	2.75
1100528	1.50
1100534	2.75
1100535	3.75
1100540	3.00
1100542	1.00
1100566	3.00
1100585	0.25
1100590	2.50
1100725	3.00
1100873	1.50
1100914	3.25
1100915	5.50
1100920	2.25
1100990	4.50
1100991	3.75

Table 42

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1101101	4.50
1101339	5.75
1101351	2.25
1101974	2.25
1101975	1.75
1102024	2.00
1102028	0.75
1102050	5.00
1102130	2.00
1102131	2.00

Table 43

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1102336	2.25
1102353	1.75
1102551	3.00
1102557	2.75
1102574	3.00
1102580	1.75
1102599	0.75
1102657	1.00
1102811	2.00
1102970	3.00
1102977	0.75
1102978	1.50
1102979	1.50
1103103	3.25

Table 44

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100379	1.50
1100398	2.00
1100399	2.75
1100408	4.00
1100409	2.50
1100521	4.00
1100527	2.00
1100536	4.50
1100541	6.00
1100544	3.00
1100839	3.00
1101000	4.00
1101920	1.75
1102329	3.25
1102666	3.00

Table 45

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100571	1.50
1100572	1.25
1100667	0.00
1100730	3.25
1100732	3.25
1100809	1.25
1100864	3.25
1100865	2.75
1100907	3.25
1100911	0.50
1100980	4.00
1101054	4.00
1101065	2.75

Table 46

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1101121	2.25
1101122	3.25
1101350	4.00
1101352	3.25
1101411	1.00
1101657	0.25
1102084	2.50
1102090	2.50
1102128	2.75
1102198	3.00
1102562	2.00
1102563	3.50
1102612	2.25
1102667	1.75

Table 47

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100410	3.50
1100468	0.25
1100557	1.00
1102541	0.75
1102600	0.50
1102637	0.00
1102677	4.00
1102683	0.25
1102725	0.50
1102980	1.25
1103001	2.75
1103014	0.50
1103069	1.00

Table 48

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.50
1100584	0.25
1100697	0.25
1100753	0.00
1100810	1.75
1100872	1.50
1100898	2.00
1100900	1.00
1100902	0.25
1100921	0.50
1100992	0.00
1101099	3.25
1101120	2.00
1101203	1.50
1101918	1.00

Table 49

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100559	0.25
1101053	0.00
1101202	0.00
1101383	0.25
1101659	0.00
1101873	0.75
1102052	0.00
1102103	0.25
1102108	0.00
1102129	0.25
1102180	0.00
1102202	0.00
1102239	0.00
1102678	0.00
1102998	2.00

Table 50

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
650528	0.50
1100429	0.00
1100430	0.00
1100434	0.25
1100666	0.25
1100756	0.00
1100802	0.50
1100863	0.00

1100906	0.25
1102379	0.50
1102598	1.75
1102646	0.00
1102663	0.00
1102669	0.00
1102679	0.00
1102750	0.00

Table 51

Tolerability scores in rats at 3 mg dose

Compound Number	**3 hour FOB**
PBS	0.00
1100369	4.00
1100479	5.00
1100505	6.00
1100508	6.00
1101375	3.00
1101721	5.75
1101853	4.00
1102690	1.25
1102706	4.50
1102808	5.00
1103041	4.75

Table 52

Tolerability scores in rats at 3 mg dose

Compound Number	**3 hour FOB**
PBS	0.00
1100505	5.00
1100506	2.25
1100729	2.25

Table 53

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100672	0.00
1100731	3.00

Table 54

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.25
1100731	4.00

Table 55

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100723	0.50
1100724	2.25
1100728	0.75

Table 56

Tolerability scores in rats at 3 mg dose

Compound Number	3 hour FOB
PBS	0.00
1100673	0.00

Example 9: Activity of modified oligonucleotides complementary to human ATXN3 in transgenic mice, multiple dose

Modified oligonucleotides described above were tested in the ATXN3 YAC transgenic mouse model which contains the full-length human ATXN3 disease gene harboring an expanded CAG repeat (CAG_{84}, Q84) previously described herein.

The ATXN3 transgenic mice were divided into groups of 4 mice each. Mice in each group were given a single ICV bolus of oligonucleotide at a dose of 10 µg, 30 µg, 100 µg, 300 µg, or 700 µg, and sacrificed two weeks later. A group of 3-4 mice was injected with PBS and served as the control group to which oligonucleotide-treated groups were compared. After two weeks, mice were sacrificed, and RNA was extracted from brain cortex, spinal cord, brain stem and/or cerebellum for real-time PCR analysis of measurement of RNA expression of ATXN3 using primer probe set RTS43981. Results are presented as percent change of RNA, relative to PBS control, normalized to mouse cyclophilin A measured using mouse primer probe set m_cyclo24 as previously described herein. As shown in the tables below, human ATXN3 RNA was reduced in various tissues. ED_{50} was calculated for the compounds using the "non-linear fit of transform ED50" formula in GraphPad Prism 7.01. In some cases, ED_{50} could not be reliably calculated and is represented as "N.C." (not calculated).

Table 57

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	Dose (µg)	Spinal Cord		Cortex		Brain Stem		Cerebellum	
		hATXN3 Expression (% control)	ED_{50} (µg)	hATXN3 Expression (% control)	ED_{50} (µg)	hATXN3 Expression (% control)	ED_{50} (µg)	hATXN3 Expression (% control)	ED_{50} (µg)
1100673	10	72	16.3	83	62.9	88	33.6	78	N.C.
	30	39		76		58		76	
	100	23		47		34		65	
	300	14		15		20		50	
	700	12		11		17		42	
1101657	10	71	25.3	93	69.9	91	79.4	94	N.C.
	30	57		76		81		77	
	100	36		45		51		77	
	300	19		23		28		49	
	700	19		17		25		44	
1102598	10	74	28.0	91	65.0	108	113.9	98	N.C.
	30	53		63		71		69	
	100	41		55		60		69	
	300	30		24		39		59	
	700	23		18		32		45	
1102811	10	76	24.7	90	80.4	93	49.5	92	N.C.
	30	47		74		67		75	
	100	30		51		41		66	
	300	17		31		25		67	
	700	11		16		18		62	

Table 58

Reduction of human ATXN3 RNA in transgenic mice

Compound Number	Dose (ug)	Spinal Cord		Cortex		Brain Stem	
		hATXN3 Expression (% control)	ED_{50} (µg)	hATXN3 Expression (% control)	ED_{50} (µg)	hATXN3 Expression (% control)	ED_{50} (µg)
1102130	10	69	21.0	76	28.6	78	33.2
	30	54		51		58	
	100	31		37		36	
	300	24		14		33	
	700	18		9		23	

Example 10: Effect of modified oligonucleotides complementary to human ATXN3 in cynomolgus monkeys following repeat-dose intrathecal injection, 13-week study

Cynomolgus monkeys are treated with modified oligonucleotides to determine the local and systemic tolerability and pharmacokinetics at 1 dose level, following 3 intrathecal lumbar bolus injections administered 4 weeks apart. Cynomolgus monkeys in groups of 4 are treated with either artificial CSF or modified oligonucleotide. Tissues are collected 1 week after the final injection.

Assessment of tolerability is based on clinical observations, body weights, food consumption, physical and neurological examinations including sensorimotor reflexes, cerebral reflexes and spinal reflexes, coagulation, hematology, clinical chemistry (blood and cerebral spinal fluid (CSF)), cell count, and anatomic pathology evaluations. Complete necropsies are performed with a recording of any macroscopic abnormality. Organ weights are taken and microscopic examinations are conducted. Blood was collected for complement analysis. In addition, blood, CSF, and tissues (at necropsy) are collected for toxicokinetic evaluations.

Activity of modified oligonucleotides is analyzed in brain and spinal cord tissue by measuring cynomolgus monkey ATXN3 RNA. Brain and spinal cord samples are collected and flash frozen in liquid nitrogen and stored frozen (-60°C to -90°C). At time of sampling, 2 mm biopsy punches are used to collect samples from frozen tissues for RNA analysis. Punches are taken from multiple brain and spinal cord regions.

Example 11. Human Clinical Trial with modified oligonucleotides complementary to human ATXN3

Ascending doses of modified oligonucleotide are evaluated in a randomized, double-blind study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics, and clinical efficacy in patients with confirmed genetic mutation in SCA3. Patient safety will be monitored closely during the study. Safety and tolerability evaluations include: physical examination and standard neurological assessment, vital signs, ECG, AEs and concomitant medications, Columbia Suicide Severity Rating Scale (C-SSRS), CSF safety labs, plasma laboratory tests, urinalysis, and neuroimaging studies.