



(51) International Patent Classification:

Not classified

(21) International Application Number:

PCT/US2023/063280

(22) International Filing Date:

24 February 2023 (24.02.2023)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/313,948 25 February 2022 (25.02.2022) US

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(81) Designated States (unless otherwise indicated, for every

kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ,

CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM,

DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,

HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE,

KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU,

LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG,

NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS,

RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS,

ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every

kind of regional protection available): ARIPO (BW, CV,

GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST,

SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ,

RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ,

DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT,

LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,

SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,

GQ, GW, KM, ML, MR, NE, SN, TD, TG).

(54) Title: COMPOUNDS AND METHODS FOR MODULATING ATN1 EXPRESSION

(57) Abstract: Provided are compounds, pharmaceutical compositions, and methods of use for reducing the amount or activity of ATN1 RNA in a cell or subject, and in certain instances reducing the amount of atrophin-1 protein in a cell or subject. Such compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a poly glutamine (polyQ) disease or disorder associated with ATN1.



COMPOUNDS AND METHODS FOR MODULATING ATN1 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 BIOL0402SEQ.xml, created on February 15, 2023, which is 2128 KB in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field

Provided are compounds, pharmaceutical compositions, and methods of use for reducing the amount or activity of ATN1 RNA in a cell or subject, and in certain instances reducing the amount of atrophin-1 protein in a cell or subject. Such compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a polyglutamine (polyQ) disease or disorder associated with ATN1. Such symptoms and hallmarks include seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on magnetic resonance imaging (MRI), hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign. Such polyQ diseases or disorders include dentatorubral-pallidoluysian atrophy (DRPLA).

Background

Dentatorubral-pallidoluysian atrophy (DRPLA) is an autosomal dominant neurodegenerative disorder that is caused by an extended CAG repeat in the *ATN1* gene, which encodes atrophin-1 protein. In certain instances, a mutation in the *ATN1* gene extends the CAG repeat to 48 times or more, resulting in an aberrant structure of atrophin-1 protein and subsequent accumulation of the protein in the neurons. The number of CAG repeats further influences the severity of the symptoms as well as the age at onset of DRPLA. For example, about 48 to 65 CAG repeats can lead to the development of adult DRPLA while a number of CAG repeats higher than 62 can lead to the development of juvenile DRPLA (Carroll, et al., "Dentatorubral-pallidoluysian Atrophy: An Update." *Tremor and other hyperkinetic movements* (New York, N.Y.), vol. 8, 577. 1 Oct. 2018).

In certain embodiments, DRPLA is characterized by a variety of symptoms and hallmarks including, but not limited to, seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, and neuronal atrophy and dysfunction. In certain embodiments, the symptoms and hallmarks include action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign. In certain embodiments, the ataxia includes progressive cerebellar ataxia, gait ataxia, limb ataxia, or truncal ataxia.

Currently there is a lack of acceptable options for treating polyglutamine (polyQ) diseases or disorders associated with ATN1 such as DRPLA. It is therefore an objective herein to provide compounds, methods, and pharmaceutical compositions for the treatment of such diseases or disorders.

Summary

Provided herein are compounds, pharmaceutical compositions, and methods of use for reducing the amount or activity of ATN1 RNA, and in certain embodiments reducing the amount of atrophin-1 protein in a cell or subject. In certain embodiments, the subject has a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the subject has DRPLA. In certain embodiments, compounds useful for reducing the amount or activity of ATN1 RNA are oligomeric compounds. In certain embodiments, compounds useful for reducing the amount or activity of atrophin-1 protein are oligomeric compounds. In certain embodiments, compounds useful for reducing the amount or activity of atrophin-1 protein are modified oligonucleotides.

Also provided are methods useful for ameliorating at least one symptom or hallmark of a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the polyglutamine (polyQ) disease or disorder associated with ATN1 is DRPLA. In certain embodiments, the symptoms or hallmarks include, but are not limited to, seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

Detailed Description

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

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

DEFINITIONS

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

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

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

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

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

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

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

As used herein, “2′-F” means a 2′-fluoro group in place of the 2′-OH group of a ribosyl sugar moiety. A “2′-F sugar moiety” or “2′-fluororibosyl sugar moiety” means a sugar moiety with a 2′-F group in place of the 2′-OH group of a ribosyl sugar moiety. Unless otherwise indicated, a 2′-F has the β-D ribosyl stereochemical configuration.

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

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

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

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

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

As used herein, “ameliorate” in reference to a treatment means improvement in at least one symptom or hallmark relative to the same symptom or hallmark in the absence of the treatment. In certain embodiments, amelioration is the reduction in the severity or frequency of a symptom or hallmark or the delayed onset or slowing of progression in the severity or frequency of a symptom or hallmark. In certain embodiments, the symptom or hallmark is seizures, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysidiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign. The progression or severity of indicators may be determined by subjective or objective measures, which are known to those skilled in the art.

As used herein, “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.

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

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

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

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

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

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

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

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

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

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

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

of a phosphorothioate internucleoside linkage. In certain embodiments, the chiral center is at the phosphorous atom of a methyl phosphoramidate internucleoside linkage.

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

As used herein, “complementary region” in reference to a region of an oligonucleotide means that at least 70% of the nucleobases of that region 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.

As used herein, “conjugate group” means a group of atoms that is directly attached to an oligonucleotide and confers at least one property to the resulting conjugated 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 covalently bound 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 sugar moiety” means a β -D ribosyl bicyclic sugar moiety wherein the second ring of the bicyclic sugar is formed via a bridge connecting the 4'-carbon and the 2'-carbon of the β -D ribosyl sugar moiety, wherein the bridge has the formula 4'-CH(CH₃)-O-2', and wherein the methyl group of the bridge is in the *S* configuration.

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

As used herein, “deoxy region” means a region of 5-12 contiguous nucleotides, wherein at least 70% of the nucleosides are 2'- β -D-deoxynucleosides. In certain embodiments, each nucleoside is selected from a 2'- β -D-

deoxynucleoside, a bicyclic nucleoside, and a 2'-substituted nucleoside. In certain embodiments, a deoxy region supports RNase H activity. In certain embodiments, a deoxy region is the gap or internal region of a gapmer.

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

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

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

As used herein, "gapmer" means a modified oligonucleotide comprising an internal region having a plurality of nucleosides that support RNase H cleavage positioned between external regions having one or more nucleosides, wherein the nucleosides comprising the internal region are chemically distinct from the nucleoside or nucleosides comprising the external regions. The internal region may be referred to as the "gap" and the external regions may be referred to as the "wings" or "wing segments." In certain embodiments, the internal region is a deoxy region. The positions of the internal region or gap refer to the order of the nucleosides of the internal region and are counted starting from the 5'-end of the internal region. Unless otherwise indicated, "gapmer" refers to a sugar motif. In certain embodiments, each nucleoside of the gap is a 2'-β-D-deoxynucleoside. In certain embodiments, the gap comprises one 2'-substituted nucleoside at position 1, 2, 3, 4, or 5 of the gap, and the remainder of the nucleosides of the gap are 2'-β-D-deoxynucleosides. As used herein, the term "MOE gapmer" indicates a gapmer having a gap comprising 2'-β-D-deoxynucleosides and wings comprising 2'-MOE nucleosides. As used herein, the term "mixed wing gapmer" indicates a gapmer having wings comprising modified nucleosides comprising at least two different sugar modifications. Unless otherwise indicated, a gapmer may comprise one or more modified internucleoside linkages and/or modified nucleobases and such modifications do not necessarily follow the gapmer pattern of the sugar modifications.

As used herein, "hotspot region" is a range of nucleobases on a target nucleic acid that is amenable to oligomeric agent or oligomeric compound-mediated reduction of the amount or activity of the target nucleic acid.

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

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

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

As used herein, “inverted sugar moiety” means the sugar moiety of an inverted nucleoside or an abasic sugar moiety having a 3' to 3' and/or 5' to 5' internucleoside linkage.

As used herein, “linked nucleosides” are nucleosides that are connected in a contiguous sequence (i.e., no additional nucleosides are presented between those that are linked).

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

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

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

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

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

As used herein, “nucleobase sequence” means the order of contiguous nucleobases in a nucleic acid or oligonucleotide, including such nucleobases that are each optionally independently modified or unmodified, and independent of any sugar or internucleoside linkage modification.

As used herein, “the nucleobase sequence of” a reference SEQ ID NO, refers only to the nucleobase sequence provided in such SEQ ID NO and therefore, does not limit sugar or internucleoside linkage modifications. Unless otherwise specified, each nucleobase may be an unmodified nucleobase, or a modified nucleobase as defined herein. For example, “A” represents unmodified or modified adenine; “C” represents unmodified or modified cytosine, “T” represents unmodified or modified thymine, “U” represents unmodified or modified uracil, and “G” represents unmodified or modified guanine. Modified nucleobases that fall outside of these definitions are represented in the sequence by a different symbol, such as an “X”. As used herein, “nucleoside” means a compound, or fragment of a compound, comprising a nucleobase and a sugar moiety. The nucleobase and sugar moiety are each, independently, unmodified or modified.

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

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

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

As used herein, “oligonucleotide” means a 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. An oligonucleotide may be paired with a second oligonucleotide that is complementary to the oligonucleotide or it may be unpaired. A “single-stranded oligonucleotide” is an unpaired oligonucleotide. A “double-stranded oligonucleotide” is an oligonucleotide that is paired with a second oligonucleotide.

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

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

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

As used herein, “population” means a plurality of molecules of identical molecular formula.

As used herein “prodrug” means a therapeutic agent in a first form outside the body that is converted to a second form within an animal or cells thereof. Typically, conversion of a prodrug within the animal is facilitated by the action of an enzymes (e.g., endogenous or viral enzyme) or chemicals present in cells or tissues and/or by physiologic conditions. In certain embodiments, the first form of the prodrug is less active than the second form.

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

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

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

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

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

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

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

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

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

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

As used herein, “stereorandom” or “stereorandom chiral center” in the context of a population of molecules of identical molecular formula means a chiral center that is not controlled during synthesis, or enriched following synthesis, for a particular absolute stereochemical configuration. The stereochemical configuration of a chiral center is considered random when it is the result of a synthetic method that is not designed to control the stereochemical configuration. For example, in a population of molecules comprising a stereorandom chiral center, the number of molecules having the (*S*) configuration of the stereorandom chiral center may be but is not necessarily the same as the number of molecules having the (*R*) configuration of the stereorandom chiral center (“racemic”). In certain embodiments, the stereorandom chiral center is not racemic because one absolute configuration predominates following synthesis, e.g., due to the action of non-chiral reagents near the enriched stereochemistry of an adjacent sugar moiety. In certain embodiments, a stereorandom chiral center is a stereorandom phosphorothioate internucleoside linkage or a mesyl phosphoramidate internucleoside linkage.

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

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

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

As used herein, “symptom or hallmark” means any physical feature or test result that indicates the existence or extent of a disease or disorder. In certain embodiments, a symptom is apparent to a subject or to a medical professional examining or testing said subject. In certain embodiments, a hallmark is apparent upon invasive diagnostic testing, including, but not limited to, post-mortem tests. In certain embodiments, symptoms and hallmarks include seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

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

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

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

As used herein, “treating” means improving a subject’s disease or condition by administering an oligomeric agent or oligomeric compound described herein. In certain embodiments, treating a subject improves a symptom relative to the same symptom in the absence of the treatment. In certain embodiments, treatment reduces in the severity or frequency of a symptom, or delays the onset of a symptom, slows the progression of a symptom, or slows the severity or frequency of a symptom.

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

CERTAIN EMBODIMENTS

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

Embodiment 1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of an ATN1 nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety 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 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 15-2443, wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

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

an equal length portion of nucleobases 6584-6607 of SEQ ID NO: 1;
 an equal length portion of nucleobases 6865-6890 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7364-7409 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7405-7430 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7484-7514 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7621-7658 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7886-7922 of SEQ ID NO: 1;
 an equal length portion of nucleobases 8763-8809 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9082-9107 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9093-9174 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9483-9525 of SEQ ID NO: 1;
 an equal length portion of nucleobases 10163-10200 of SEQ ID NO: 1;
 an equal length portion of nucleobases 11033-11081 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12214-12244 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12360-12400 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12929-12957 of SEQ ID NO: 1;
 an equal length portion of nucleobases 13300-13330 of SEQ ID NO: 1;
 an equal length portion of nucleobases 14061-14097 of SEQ ID NO: 1;
 an equal length portion of nucleobases 18284-18363 of SEQ ID NO: 1;
 an equal length portion of nucleobases 18658-18689 of SEQ ID NO: 1; or
 an equal length portion of nucleobase ranges disclosed in Table 1;

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

Embodiment 4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 528, 2437, 2296, 483, and 2137;

SEQ ID NOs: 1329, 1241, 1166, 459, 70, and 1116;

SEQ ID NOs: 770, 699, 2100, 2027, 677, 1942, 606, 527, 841, 1799, 769, 716, 654, 605, 492, 876, 1719, and 799;

SEQ ID NOs: 1626, 1557, 1486, 1412, 1337, 1251, and 1187;

SEQ ID NOs: 948, 651, 2410, 2316, 2205, 2163, 2073, 2003, 1961, 1872, and 1782;

SEQ ID NOs: 2200, 2155, 583, 2434, 2115, 2028, 1914, 1888, 1747, 1693, 1659, 1532, 1493, 1367, 1346, 1262, 1172, 460, and 71;

SEQ ID NOs: 1632, 1587, 1452, 1434, 1301, 1260, 1140, 1095, 1021, 960, 2362, 2306, 2224, and 2160;

SEQ ID NOs: 1711, 1635, 1524, 1502, 1385, 1296, 1276, 150, 228, 1093, 985, 907, 306, and 2278;

SEQ ID NOs: 1970, 1896, 765, 694, 1801, 643, and 590;

SEQ ID NOs: 867, 812, 464, 1288, 704, 1215, 75, 1191, 153, 231, 562, 548, 1060, 861, 834, 1029, 690, 680, 309, and 387;

SEQ ID NOs: 625, 1359, 1244, 2440, 1150, 1091, 1032, 929, 2413, 2300, and 2259;

SEQ ID NOs: 634, 581, 543, 863, 809, 721, 669, 157, and 235;

SEQ ID NOs: 94, 172, 681, 250, 502, 927, 878, 792, 732, 328, 406, 2355, 573, 538, 2272, 902, 827, and 740;

SEQ ID NOs: 779, 741, 2370, 645, 2309, 594, 499, 903, 775, and 738;

SEQ ID NOs: 2053, 2032, 1925, 1821, 1780, 1696, 1613, 176, 254, 332, 1499, 410, 21, 99, 518, 177, and 255;

SEQ ID NOs: 2110, 181, 1993, 259, 337, 1847, 1746, 711, and 415;

SEQ ID NOs: 2283, 2198, 2139, 2062, 1981, 1909, 1860, 416, 1695, 1622, and 1567;

SEQ ID NOs: 1553, 34, 1480, 112, 1331, 190, 1165, 1075, 1059, 982, 2365, 2299, 2243, 2157, 2097, 1982, 1943, and 1858;

SEQ ID NOs: 584, 551, 887, 800, 702, 637, 591, 201, 279, 494, 357, 435, 865, 46, 124, 202, 280, and 358;

SEQ ID NOs: 895, 764, 691, 678, 438, 49, 874, 828, 754, 127, 205, and 561; and

SEQ ID NOs: 870, 819, 1278, 1151, 1066, 1205, 1114, 748, 304, 1771, 1732, 1595, 1526, 1508, 149, 1390, 227, 1248, 2085, 2030, 1959, 1730, 1611, 1520, 739, 665, 604, 509, 844, 152, 1457, 1387, 1297, 1216, 1188, 1097, 1016, 2284, 787, 757, 2250, 308, 386, 2153, 627, 615, 510, 905, 2197, 465, 2091, 1976, 1953, 833, 729, 666, 597, 530, 629, 613, 519, 890, 832, 1212, 689, 676, 807, 713, 664, 612, 511, 836, 777, 709, 683, 557, 983, 512, 1286, 411, 22, 100, 2074, 1992, 1939, 1825, 791, 752, 1809, 1722, 1607, 1528, 569, 537, 858, 1369, 816, 717, 659, 1109, 1014, 962, 2368, 258, 2212, 2130, 2071, 1977, 182, 1703, 1592, 1565, 1462, 1371, 1292, 1245, 1200, 1101, 996, 964, 2114, 2024, 1938, 1889, 1839, 1742, 614, 1727, 267, 839, 785, 351, 429, 761, 40, 1853, 1802, 118, 1682, 196, 1537, 1498, 1407, 1321, 679, 601, 549, 853, 547, 899, 2358, 2335, 2202, 2189, 359, 2004, and 437.

Embodiment 5. The oligomeric compound of any of embodiments 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length

portion of a ATN1 nucleic acid, wherein the ATN1 nucleic acid has the nucleobase sequence of SEQ ID NO: 1 or SEQ ID NO: 2.

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

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

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

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

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

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

Embodiment 12. The oligomeric compound of embodiment 11, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, or a 2'-F sugar moiety.

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

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

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

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

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

Embodiment 18. The oligomeric compound of any of embodiments 1-17, wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage

Embodiment 19. The oligomeric compound of any of embodiments 16-18, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.

Embodiment 20. The oligomeric compound of any of embodiments 1-19, wherein at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, or 19 internucleoside linkages of the modified oligonucleotide are phosphorothioate internucleoside linkages.

Embodiment 21. The oligomeric compound of any of embodiments 1-20, wherein the modified oligonucleotide comprises an internucleoside linkage motif (from 5' to 3') selected from sosossssssssooss and soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

5 Embodiment 22. The oligomeric compound of any of embodiments 1-21, wherein the modified oligonucleotide comprises at least one modified nucleobase.

Embodiment 23. The oligomeric compound of embodiment 22, wherein the modified nucleobase is a 5-methylcytosine.

Embodiment 24. The oligomeric compound of embodiment 23, wherein each cytosine is a 5-methylcytosine.

10 Embodiment 25. The oligomeric compound of any of embodiments 1-24, wherein the modified oligonucleotide comprises a deoxy region.

Embodiment 26. The oligomeric compound of embodiment 25, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.

15 Embodiment 27. The oligomeric compound of embodiment 25 or embodiment 26, wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.

Embodiment 28. The oligomeric compound of any of embodiments 25-27, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.

20 Embodiment 29. The oligomeric compound of any of embodiments 24-27, wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein at least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 30. The oligomeric compound of embodiment 29, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.

25 Embodiment 31. The oligomeric compound of embodiment 29 or embodiment 30, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 32. The oligomeric compound of any of embodiments 1-31, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22, or 18-20 linked nucleosides, or a pharmaceutically acceptable salt thereof.

30 Embodiment 33. The oligomeric compound of any of embodiments 1-32, wherein the modified oligonucleotide consists of 20 linked nucleosides, or a pharmaceutically acceptable salt thereof.

Embodiment 34. The oligomeric compound of embodiment 31 or embodiment 33, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.

Embodiment 35. The oligomeric compound of any of embodiments 1-34, wherein the modified oligonucleotide consists of 20 linked nucleosides.

35 Embodiment 36. The oligomeric compound of any of embodiments 1-25, wherein the modified oligonucleotide comprises:

- a 5'-region consisting of 1-6 linked 5'-region nucleosides;
- a central region consisting of 6-10 linked central region nucleosides; and
- a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein

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

Embodiment 37. The oligomeric compound of any of embodiments 1-36, wherein the modified oligonucleotide comprises:

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

10 Embodiment 38. The oligomeric compound of embodiment 35, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety, and
15 each of the central region nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety.

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

Embodiment 40. The oligomeric compound of any of embodiments 1-38, wherein the oligomeric compound comprises a conjugate group.

20 Embodiment 41. The oligomeric compound of embodiment 40, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

Embodiment 42. The oligomeric compound of embodiment 41, wherein the conjugate linker is a phosphodiester linker.

Embodiment 43. The oligomeric compound of embodiment 41, wherein the conjugate linker consists of a
25 single bond.

Embodiment 44. The oligomeric compound of any of embodiments 41-43, wherein the conjugate linker is cleavable.

Embodiment 45. The oligomeric compound of any of embodiments 41-44, wherein the conjugate linker comprises 1-3 linker-nucleosides.

30 Embodiment 46. The oligomeric compound of any of embodiments 40-45, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

Embodiment 47. The oligomeric compound of any of embodiments 40-45, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 48. The oligomeric compound of any of embodiments 1-47, wherein the oligomeric compound
35 comprises a terminal group.

Embodiment 49. The oligomeric compound of any of embodiments 1-40 or 46-48, wherein the oligomeric compound does not comprise linker-nucleosides.

Embodiment 50. A chirally enriched population of oligomeric compounds of any of embodiments 1-49, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

Embodiment 51. The chirally enriched population of embodiment 50, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (Sp) configuration.

Embodiment 52. The chirally enriched population of embodiment 50, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (Rp) configuration.

Embodiment 53. The chirally enriched population of embodiment 50, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

Embodiment 54. The chirally enriched population of embodiment 50, wherein the population is enriched for modified oligonucleotides having the (Sp) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (Rp) configuration at each phosphorothioate internucleoside linkage.

Embodiment 55. The chirally enriched population of embodiment 50, 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 56. The chirally enriched population of embodiment 50, 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 57. A population of oligomeric compounds of any of embodiments 1-49, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

Embodiment 58. An oligomeric duplex comprising a first oligomeric compound and a second oligomeric compound comprising a second modified oligonucleotide, wherein the first oligomeric compound is an oligomeric compound of any of embodiments 1-49.

Embodiment 59. The oligomeric duplex of embodiment 58, wherein the second modified oligonucleotide consists of 12 to 50 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 12 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

Embodiment 60. The oligomeric duplex of embodiment 58 or embodiment 59, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.

Embodiment 61. The oligomeric duplex of embodiment 61, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.

Embodiment 62. The oligomeric duplex of any of embodiments 58-61, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.

Embodiment 63. The oligomeric duplex of embodiment 62, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.

Embodiment 64. The oligomeric duplex of embodiment 63, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂-; and -O-CH(CH₃)-.

Embodiment 65. The oligomeric duplex of embodiment 62, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.

5 Embodiment 66. The oligomeric duplex of embodiment 65, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-OMe sugar moiety or a 2'-F sugar moiety.

Embodiment 67. The oligomeric duplex of any of embodiments 62-66, wherein at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate.

10 Embodiment 68. The oligomeric duplex of any of embodiments 58-67, wherein the second modified oligonucleotide comprises at least one modified internucleoside linkage.

Embodiment 69. The oligomeric duplex of embodiment 68, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

15 Embodiment 70. The oligomeric duplex of embodiment 68, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester and a phosphorothioate internucleoside linkage.

Embodiment 71. The oligomeric duplex of any of embodiments 58-70, wherein the second modified oligonucleotide comprises at least one modified nucleobase.

Embodiment 72. The oligomeric duplex of embodiment 71, wherein the at least one modified nucleobase is 5-methylcytosine.

20 Embodiment 73. The oligomeric duplex of any of embodiments 58-72, wherein the second oligomeric compound comprises a conjugate group.

Embodiment 74. The oligomeric duplex of embodiment 73, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

25 Embodiment 75. The oligomeric duplex of embodiment 74, wherein the conjugate linker consists of a single bond.

Embodiment 76. The oligomeric duplex of embodiment 74 or embodiment 75, wherein the conjugate linker is cleavable.

Embodiment 77. The oligomeric duplex of any of embodiments 74-76, wherein the conjugate linker comprises 1-3 linker-nucleosides.

30 Embodiment 78. The oligomeric duplex of any of embodiments 74-77, wherein the conjugate linker is a phosphodiester linker.

Embodiment 79. The oligomeric duplex of any of embodiments 73-78, wherein the conjugate group is attached to the 5'-end of the second modified oligonucleotide.

35 Embodiment 80. The oligomeric duplex of any of embodiments 73-78, wherein the conjugate group is attached to the 3'-end of the second modified oligonucleotide.

Embodiment 81. The oligomeric duplex of any of embodiments 73-78, wherein the conjugate group is attached via the 2' position of a ribosyl sugar moiety at an internal position of the second modified oligonucleotide.

Embodiment 82. The oligomeric duplex of any of embodiments 73-81, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13

alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

Embodiment 83. The oligomeric duplex of any of embodiments 73-82, wherein the conjugate group comprises a cell-targeting moiety.

Embodiment 84. The oligomeric duplex of any of embodiments 58-83, wherein the second modified oligonucleotide comprises a terminal group.

Embodiment 85. The oligomeric duplex of embodiment 74, wherein the terminal group is an abasic sugar moiety.

Embodiment 86. An antisense agent comprising or consisting of an antisense compound, wherein the antisense compound is the oligomeric compound of any of embodiments 1-49.

Embodiment 87. An antisense agent, wherein the antisense agent is the oligomeric duplex of any of embodiments 56-83.

Embodiment 88. The antisense agent of embodiment 86 or embodiment 87, wherein the antisense agent is:

i) an RNase H agent capable of reducing the amount of ATN1 nucleic acid through the activation of RNase H; or

ii) an RNAi agent capable of reducing the amount of ATN1 nucleic acid through the activation of RISC/Ago2.

Embodiment 89. The antisense agent of any of embodiments 86-88, wherein the antisense agent comprises a conjugate group, and wherein the conjugate group comprises a cell-targeting moiety.

Embodiment 90. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, or an antisense agent of any of embodiments 86-89, and a pharmaceutically acceptable diluent.

Embodiment 91. The pharmaceutical composition of embodiment 90, wherein the pharmaceutically acceptable diluent is phosphate buffered saline (PBS) or artificial CSF (aCSF).

Embodiment 92. The pharmaceutical composition of embodiment 91, wherein the pharmaceutical composition consists essentially of the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, or the antisense agent, and aCSF.

Embodiment 93. The pharmaceutical composition of embodiment 91, wherein the pharmaceutical composition consists essentially of the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, or the antisense agent, and PBS.

Embodiment 94. A method comprising administering to a subject an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, an antisense agent of any of embodiments 86-89, or a pharmaceutical composition of any of embodiments 90-93.

Embodiment 95. A method of treating a polyglutamine (polyQ) disease or disorder associated with ATN1 comprising administering to a subject having or at risk for developing the polyQ disease or disorder associated with ATN1 a therapeutically effective amount of an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, an antisense

agent of any of embodiments 86-89, or a pharmaceutical composition of any of embodiments 90-93; thereby treating the polyQ disease or disorder associated with ATN1.

Embodiment 96. The method of embodiment 95, wherein the polyQ disease or disorder associated with ATN1 is dentatorubral-pallidoluysian atrophy (DRPLA).

Embodiment 97. The method of embodiment 95 or 96, wherein at least one symptom or hallmark of the polyQ disease or disorder associated with ATN1 is ameliorated.

Embodiment 98. The method of embodiment 97, wherein the symptom or hallmark is seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

Embodiment 99. The method of embodiment 97 or embodiment 97, wherein administering the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition reduces or delays the onset or progression of seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

Embodiment 100. The method of any of embodiments 94-99, wherein the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition is administered to the central nervous system or systemically.

Embodiment 101. The method of embodiment 100, wherein the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition is administered intrathecally.

Embodiment 102. The method of any of embodiments 94-101, wherein the subject is a human.

Embodiment 103. A method of reducing expression of ATN1 in a cell comprising contacting the cell with an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, an antisense agent of any of embodiments 86-89, or a pharmaceutical composition of any of embodiments 90-93.

Embodiment 104. The method of embodiment 103, wherein the cell is a brain cell.

Embodiment 105. The method of embodiment 103 or embodiment 104, wherein the cell is a human cell.

Embodiment 106. Use of an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, an antisense agent of any of embodiments 86-89, or a pharmaceutical composition of any of embodiments 90-93 for treating a polyglutamine (polyQ) disease or disorder associated with ATN1.

Embodiment 107. Use of an oligomeric compound of any of embodiments 1-49, a population of oligomeric compounds of any of embodiments 50-57, an oligomeric duplex of any of embodiments 58-85, an antisense agent of any

of embodiments 86-89, or a pharmaceutical composition of any of embodiments 90-93 in the manufacture of a medicament for treating a polyglutamine (polyQ) disease or disorder associated with ATN1.

Embodiment 108. The use of embodiment 106 or embodiment 107, wherein the polyglutamine (polyQ) disease or disorder associated with ATN1 is dentatorubral-pallidolusian atrophy (DRPLA).

5

I. Certain Oligonucleotides

In certain embodiments, provided herein are oligomeric compounds comprising oligonucleotides, which consist of linked nucleosides. Oligonucleotides may be unmodified oligonucleotides (RNA or DNA) or may be modified oligonucleotides. Modified oligonucleotides comprise at least one modification relative to unmodified RNA or DNA.

10 That is, modified oligonucleotides comprise at least one modified nucleoside (comprising a modified sugar moiety and/or a modified nucleobase) and/or at least one modified internucleoside linkage. Certain modified nucleosides and modified internucleoside linkages suitable for use in modified oligonucleotides are described below.

A. Certain Modified Nucleosides

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

1. Certain Sugar Moieties

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

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

30 In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 2'-position. Examples of substituent groups suitable for the 2'-position of modified sugar moieties include but are not limited to: -F, -OCH₃ ("OMe" or "O-methyl"), and -OCH₂CH₂OCH₃ ("MOE" or "O-methoxyethyl"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF₃, OCF₃, O-C₁-C₁₀ alkoxy, O-C₁-C₁₀ substituted alkoxy, O-C₁-C₁₀ alkyl, O-C₁-C₁₀ substituted alkyl, S-alkyl, N(R_m)-alkyl, O-alkenyl, S-alkenyl, N(R_m)-alkenyl, O-alkynyl, S-alkynyl, N(R_m)-alkynyl, O-alkynyl-O-alkyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, O(CH₂)₂SCH₃, O(CH₂)₂ON(R_m)(R_n) or OCH₂C(=O)-N(R_m)(R_n), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C₁-C₁₀ alkyl, -O(CH₂)₂ON(CH₃)₂ ("DMAOE"), 2'-O(CH₂)₂O(CH₂)₂N(CH₃)₂ ("DMAEOE"), and the 2'-substituent groups described in Cook et al., U.S. 6,531,584; Cook et al., U.S. 5,859,221; and Cook et al., U.S. 6,005,087. Certain embodiments of these 2'-substituent groups can be further substituted with one or more substituent groups independently selected from among: hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro (NO₂), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl.

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, NH₂, N₃, OCF₃, OCH₃, O(CH₂)₃NH₂, CH₂CH=CH₂,

$\text{OCH}_2\text{CH}=\text{CH}_2$, $\text{OCH}_2\text{CH}_2\text{OCH}_3$ ("MOE"), $\text{O}(\text{CH}_2)_2\text{SCH}_3$, $\text{O}(\text{CH}_2)_2\text{ON}(\text{R}_m)(\text{R}_n)$, $\text{O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$, and N-substituted acetamide ($\text{OCH}_2\text{C}(=\text{O})-\text{N}(\text{R}_m)(\text{R}_n)$), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted $\text{C}_1\text{-C}_{10}$ 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 , $\text{OCH}_2\text{CH}_2\text{OCH}_3$, $\text{O}(\text{CH}_2)_2\text{SCH}_3$, $\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$, $\text{O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$, $\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$ ("DMAOE"), $\text{O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$ ("DMAEOE"), and $\text{OCH}_2\text{C}(=\text{O})-\text{N}(\text{H})\text{CH}_3$ ("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 , $\text{OCH}_2\text{CH}_2\text{OCH}_3$, $\text{O}(\text{CH}_2)_2\text{SCH}_3$, $\text{O}(\text{CH}_2)_2\text{ON}(\text{CH}_3)_2$, $\text{O}(\text{CH}_2)_2\text{O}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$, and $\text{OCH}_2\text{C}(=\text{O})-\text{N}(\text{H})\text{CH}_3$ ("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 $\text{OCH}_2\text{CH}_2\text{OCH}_3$.

In certain embodiments, modified furanosyl sugar moieties and nucleosides incorporating such modified furanosyl sugar moieties are further defined by isomeric configuration. For example, a 2'-deoxyfuranosyl sugar moiety may be in seven isomeric configurations other than the naturally occurring β -D-deoxyribose configuration. Such modified sugar moieties are described in, e.g., WO 2019/157531, incorporated by reference herein. A 2'-modified sugar moiety has an additional stereocenter at the 2'-position relative to a 2'-deoxyfuranosyl sugar moiety; therefore, such sugar moieties have a total of sixteen possible isomeric configurations. 2'-modified sugar moieties described herein are in the β -D-ribose isomeric configuration unless otherwise specified.

In certain embodiments, non-bicyclic modified sugar moieties comprise a substituent group at the 4'-position. Examples of substituent groups suitable for the 4'-position of modified sugar moieties include but are not limited to alkoxy (e.g., methoxy), alkyl, and those described in Manoharan et al., WO2015/106128.

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

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

In certain embodiments, non-bicyclic modified sugar moieties comprise more than one non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties and the modified sugar moieties and modified nucleosides described in Migawa et al., WO 2008/101157 and Rajeev et al., US2013/0203836).

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

Certain modified sugar moieties comprise a substituent that bridges two atoms of the furanosyl ring to form a second ring, resulting in a bicyclic sugar moiety. In certain embodiments, the bicyclic sugar moiety comprises a bridge between the 4' and the 2' furanose ring atoms. Examples of such 4' to 2' bridging sugar substituents include, but are not limited to: 4'- 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(CH₃)-O-2' (referred to as "constrained ethyl" or "cEt"), 4'-CH₂-O-CH₂-2', 4'-CH₂-N(R)-2', 4'-CH(CH₂OCH₃)-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(CH₃)(CH₃)-O-2' and analogs thereof (*see, e.g.*, Seth et al., U.S. 8,278,283), 4'-CH₂-N(OCH₃)-2' and analogs thereof (*see, e.g.*, Prakash et al., U.S. 8,278,425), 4'-CH₂-O-N(CH₃)-2' (*see, e.g.*, Allerson et al., U.S. 7,696,345 and Allerson et al., U.S. 8,124,745), 4'-CH₂-C(H)(CH₃)-2' (*see, e.g.*, Zhou, et al., *J. Org. Chem.*, 2009, 74, 118-134), 4'-CH₂-C(=CH₂)-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'-CH₂-O-N(R)-2', and 4'-CH₂-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C₁-C₁₂ alkyl (*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;

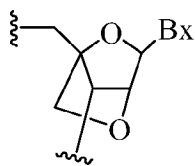
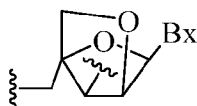
n is 1, 2, 3, or 4;

each R_a and R_b is, independently, H, a protecting group, hydroxyl, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, substituted C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, substituted C₂-C₁₂ alkynyl, C₅-C₂₀ aryl, substituted C₅-C₂₀ aryl, heterocycle radical, substituted heterocycle radical, heteroaryl, substituted heteroaryl, C₅-C₇ alicyclic radical, substituted C₅-C₇ alicyclic radical, halogen, OJ₁, NJ₁J₂, SJ₁, N₃, COOJ₁, acyl (C(=O)-H), substituted acyl, CN, sulfonyl (S(=O)₂-J₁), or sulfoxyl (S(=O)-J₁); and

each J₁ and J₂ is, independently, H, C₁-C₁₂ alkyl, substituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, substituted C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, substituted C₂-C₁₂ alkynyl, C₅-C₂₀ aryl, substituted C₅-C₂₀ aryl, acyl (C(=O)-H), substituted acyl, a heterocycle radical, a substituted heterocycle radical, C₁-C₁₂ aminoalkyl, substituted C₁-C₁₂ 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; Alback 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; Wahlestedt et al., *Proc. Natl. Acad. Sci. U. S. A.*, 2000, 97, 5633-5638; 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.*, 2007, 129, 8362-8379; Elayadi et al., *Curr. Opinion Inven. Drugs*, 2001, 2, 558-561; Braasch et al., *Chem. Biol.*, 2001, 8, 1-7; Orum et al., *Curr. Opinion Mol. Ther.*, 2001, 3, 239-243; Wengel et al., 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; 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.

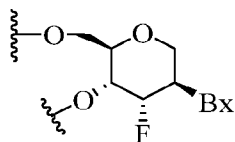
LNA (β -D-configuration)bridge = 4'-CH₂-O-2' α -L-LNA (α -L-configuration)bridge = 4'-CH₂-O-2'

α -L-methyleneoxy (4'-CH₂-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). The addition of locked nucleic acids to siRNAs has been shown to increase siRNA stability in serum, and to reduce off-target effects (Elmen, J. et al., (2005) *Nucleic Acids Research* 33(1):439-447; Mook, OR. et al., (2007) *Mal Cane Ther* 6(3):833-843; Grunweller, A. et al., (2003) *Nucleic Acids Research* 31(12):3185-3193). Herein, general descriptions of bicyclic nucleosides include both isomeric configurations. When the positions of specific bicyclic nucleosides (e.g., LNA or cEt) are identified in exemplified embodiments herein, they are in the 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).

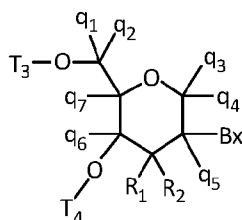
In certain embodiments, modified sugar moieties are sugar surrogates. In certain such embodiments, the oxygen atom of the sugar moiety is replaced, e.g., with a sulfur, carbon or nitrogen atom. In certain such embodiments, such modified sugar moieties also comprise bridging and/or non-bridging substituents 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"), mannitol 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;

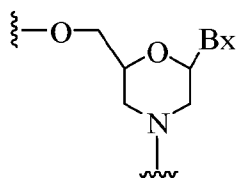
T₃ and T₄ are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T₃ and T₄ is an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T₃ and T₄ is H, a hydroxyl protecting group, a linked conjugate group, or a 5' or 3'-terminal group;

q₁, q₂, q₃, q₄, q₅, q₆ and q₇ are each, independently, H, C₁-C₆ alkyl, substituted C₁-C₆ alkyl, C₂-C₆ alkenyl, substituted C₂-C₆ alkenyl, C₂-C₆ alkynyl, or substituted C₂-C₆ alkynyl; and

each of R₁ and R₂ is independently selected from among hydrogen, halogen, substituted or unsubstituted alkoxy, NJ₁J₂, SJ₁, N₃, OC(=X)J₁, OC(=X)NJ₁J₂, NJ₃C(=X)NJ₁J₂, and CN, wherein X is O, S or NJ₁, and each J₁, J₂, and J₃ is, independently, H or C₁-C₆ alkyl.

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

In certain embodiments, sugar surrogates comprise rings having more than 5 atoms and more than one heteroatom. For example, nucleosides comprising morpholino sugar moieties and their use in oligonucleotides have been reported (*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 referred to herein as “modified morpholinos.”

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

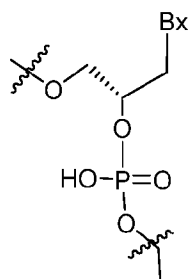
2013, 11, 5853-5865), and nucleosides and oligonucleotides described in Manoharan et al., US2013/130378.

Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos. 5,539,082; 5,714,331; and 5,719,262. Additional PNA compounds suitable for use in the oligonucleotides of the invention are described in, for example, in Nielsen *et al.*, *Science*, 1991, 254, 1497-1500.

In certain embodiments, sugar surrogates are the “unlocked” sugar structure of UNA (unlocked nucleic acid) nucleosides. UNA is an unlocked acyclic nucleic acid, wherein any of the bonds of the sugar has been removed, forming an unlocked sugar surrogate. Representative U.S. publications that teach the preparation of UNA include, but are not limited to, US Patent No. 8,314,227; and US Patent Publication Nos. 2013/0096289; 2013/0011922; and 2011/0313020, the entire contents of each of which are hereby incorporated herein by reference.

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

(S)-GNA



where Bx represents any nucleobase.

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

2. Certain Modified Nucleobases

In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising an unmodified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside comprising a modified nucleobase. In certain embodiments, modified oligonucleotides comprise one or more nucleoside that does not comprise a nucleobase, referred to as an abasic nucleoside. In certain embodiments, modified oligonucleotides comprise one or more inosine nucleosides (i.e., nucleosides comprising a hypoxanthine nucleobase).

In certain embodiments, modified nucleobases are selected from: 5-substituted pyrimidines, 6-azapyrimidines, alkyl or alkynyl substituted pyrimidines, alkyl substituted purines, and N-2, N-6 and O-6 substituted purines. In certain embodiments, modified nucleobases are selected from: 5-methylcytosine, 2-aminopropyladenine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-N-methylguanine, 6-N-methyladenine, 2-propyladenine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-propynyl ($\text{-C}\equiv\text{C-CH}_3$) 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-

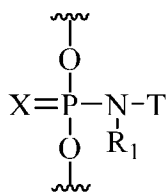
benzoylcytosine, 5-methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. Further modified nucleobases include tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one and 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2-one (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., US 2003/0158403; Manoharan et al., US 2003/0175906; 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., U.S. 6,166,199; and Matteucci et al., U.S. 6,005,096.

3. Certain Modified Internucleoside Linkages

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

In certain embodiments, a modified internucleoside linkage is any of those described in WO 2021/030778, incorporated by reference herein. In certain embodiments, a modified internucleoside linkage comprises the formula:



wherein independently for each internucleoside linking group of the modified oligonucleotide:

X is selected from O or S;

R₁ is selected from H, C₁-C₆ alkyl, and substituted C₁-C₆ alkyl; and

5 T is selected from SO₂R₂, C(=O)R₃, and P(=O)R₄R₅, wherein:

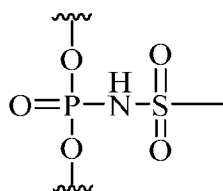
R₂ is selected from an aryl, a substituted aryl, a heterocycle, a substituted heterocycle, an aromatic heterocycle, a substituted aromatic heterocycle, a diazole, a substituted diazole, a C₁-C₆ alkoxy, C₁-C₆ alkyl, C₁-C₆ alkenyl, C₁-C₆ alkynyl, substituted C₁-C₆ alkyl, substituted C₁-C₆ alkenyl substituted C₁-C₆ alkynyl, and a conjugate group;

R₃ is selected from an aryl, a substituted aryl, CH₃, N(CH₃)₂, OCH₃ and a conjugate group;

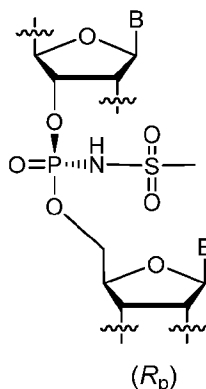
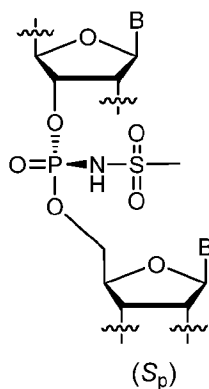
10 R₄ is selected from OCH₃, OH, C₁-C₆ alkyl, substituted C₁-C₆ alkyl and a conjugate group; and

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

In certain embodiments, a modified internucleoside linkage comprises a mesyl phosphoramidate linking group having a formula:



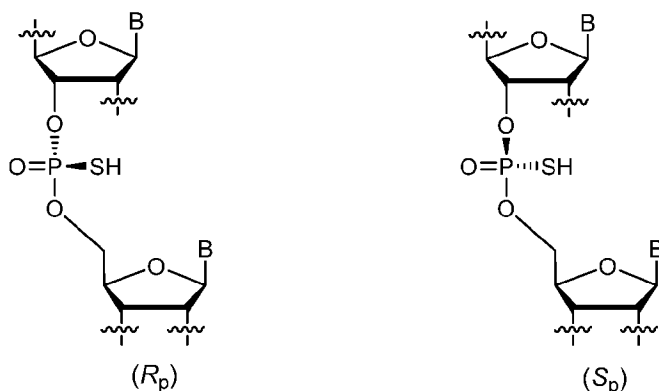
15 In certain embodiments, a mesyl phosphoramidate internucleoside linkage may comprise a chiral center. In certain embodiments, modified oligonucleotides comprising (*R*_p) and/or (*S*_p) mesyl phosphoramidates comprise one or more of the following formulas, respectively, wherein "B" indicates a nucleobase:



20 Representative internucleoside linkages having a chiral center include but are not limited to alkylphosphonates, phosphoramidates, 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, 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.

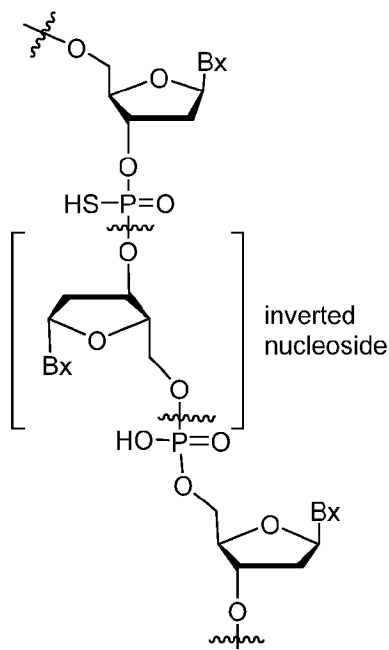
In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 65% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 70% of the molecules in 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 (*Sp*) configuration. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one phosphorothioate in the (*Rp*) configuration. In certain embodiments, modified oligonucleotides comprising (*Rp*) and/or (*Sp*) phosphorothioates comprise one or more of the following formulas, respectively, wherein "B" indicates a nucleobase:



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'-CH₂-N(CH₃)-O-5'), amide-3 (3'-CH₂-C(=O)-N(H)-5'), amide-4 (3'-CH₂-N(H)-C(=O)-5'), formacetal (3'-O-CH₂-O-5'), methoxypropyl (MOP), and thioformacetal (3'-S-CH₂-O-5'). Further neutral internucleoside linkages include nonionic linkages comprising siloxane (dialkylsiloxane), carboxylate ester, carboxamide, sulfide, sulfonate ester and amides (See for example: *Carbohydrate Modifications in Antisense Research*; Y.S. Sanghvi and P.D. Cook, Eds., ACS Symposium Series 580; Chapters 3 and 4, 40-65). Further neutral internucleoside linkages include nonionic linkages comprising mixed N, O, S and CH₂ component parts.

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

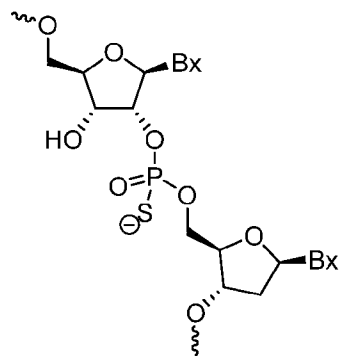


wherein each Bx independently represents any nucleobase.

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

In certain embodiments, such groups lack a nucleobase and are referred to herein as inverted sugar moieties. In certain embodiments, an inverted sugar moiety is terminal (i.e., attached to the last nucleoside on one end of an oligonucleotide) and so only one internucleoside linkage above will be present. In certain such embodiments, additional features (such as a conjugate group) may be attached to the inverted sugar moiety. Such terminal inverted sugar moieties can be attached to either or both ends of an oligonucleotide.

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



wherein each Bx represents any nucleobase.

B. Certain Motifs

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

1. Certain Sugar Motifs

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

In certain embodiments, modified oligonucleotides comprise or consist of a region having a gapmer motif, which is defined by two external regions or “wings” and a central or internal region or “gap.” The three regions of a gapmer motif (the 5'-wing, the gap, and the 3'-wing) form a contiguous sequence of nucleosides wherein at least some of the sugar moieties of the nucleosides of each of the wings differ from at least some of the sugar moieties of the nucleosides of the gap. Specifically, at least the sugar moieties of the nucleosides of each wing that are closest to the gap (the 3'-most nucleoside of the 5'-wing and the 5'-most nucleoside of the 3'-wing) differ from the sugar moiety of the neighboring gap nucleosides, thus defining the boundary between the wings and the gap (i.e., the wing/gap junction). In certain embodiments, the sugar moieties within the gap are the same as one another. In certain embodiments, the gap includes one or more nucleoside having a sugar moiety that differs from the sugar moiety of one or more other nucleosides of the gap. In certain embodiments, the sugar motifs of the two wings are the same as one another (symmetric gapmer). In certain embodiments, the sugar motif of the 5'-wing differs from the sugar motif of the 3'-wing (asymmetric gapmer).

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

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

In certain embodiments, the gapmer is a deoxy gapmer. In certain embodiments, the nucleosides on the gap side of each wing/gap junction comprise 2'-β-D-deoxyribose sugar moieties and the nucleosides on the wing sides of each

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

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

Herein, the lengths (number of nucleosides) of the three regions of a gapmer may be provided using the notation [# of nucleosides in the 5'-wing] – [# of nucleosides in the gap] – [# of nucleosides in the 3'-wing]. Thus, a 3-10-3 gapmer consists of 3 linked nucleosides in each wing and 10 linked nucleosides in the gap. Where such nomenclature is followed by a specific modification, that modification is the modification in each sugar moiety of each wing and the gap nucleosides comprise 2'-β-D-deoxyribose sugar moieties. Thus, a 5-10-5 MOE gapmer consists of 5 linked 2'-MOE nucleosides in the 5'-wing, 10 linked 2'-β-D-deoxynucleosides in the gap, and 5 linked 2'-MOE nucleosides in the 3'-wing. A 3-10-3 cEt gapmer consists of 3 linked cEt nucleosides in the 5'-wing, 10 linked 2'-β-D-deoxynucleosides in the gap, and 3 linked cEt nucleosides in the 3'-wing. A 5-8-5 gapmer consists of 5 linked nucleosides comprising a modified sugar moiety in the 5'-wing, 8 linked 2'-β-D-deoxynucleosides in the gap, and 5 linked nucleosides comprising a modified sugar moiety in the 3'-wing. A 5-8-5 mixed gapmer has at least two different modified sugar moieties in the 5'- and/or the 3'-wing.

In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 BNA gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 cEt gapmers. In certain embodiments, modified oligonucleotides are 3-10-3 LNA gapmers.

In certain embodiments, modified oligonucleotides have a sugar motif of 5'-eeeeeeeeeeeeeeee-3', wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, each "e" represents a 2'-MOE sugar moiety.

2. Certain Nucleobase Motifs

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

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

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

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 (Sp) phosphorothioate, and a (Rp) phosphorothioate.

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

In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

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

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 $X \leq Y$. For example, in certain embodiments, oligonucleotides consist of 12 to 13, 12 to 14, 12 to 15, 12 to 16, 12 to 17, 12 to 18, 12 to 19, 12 to 20, 12 to 21, 12 to 22, 12 to 23, 12 to 24, 12 to 25, 12 to 26, 12 to 27, 12 to 28, 12 to 29, 12 to 30, 13 to 14, 13 to 15, 13 to 16, 13 to 17, 13 to 18, 13 to 19, 13 to 20, 13 to 21, 13 to 22, 13 to 23, 13 to 24, 13 to 25, 13 to 26, 13 to 27, 13 to 28, 13 to 29, 13 to 30, 14 to 15, 14 to 16, 14 to 17, 14 to 18, 14 to 19, 14 to 20, 14 to 21, 14 to 22, 14 to 23, 14 to 24, 14 to 25, 14 to 26, 14 to 27, 14 to 28, 14 to 29, 14 to 30, 15 to 16, 15 to 17, 15 to 18, 15 to 19, 15 to 20, 15 to 21, 15 to 22, 15 to 23, 15 to 24, 15 to 25, 15 to 26, 15 to 27, 15 to 28, 15 to 29, 15 to 30, 16 to 17, 16 to 18, 16 to 19, 16 to 20, 16 to 21, 16 to 22, 16 to 23, 16 to 24, 16 to 25, 16 to 26, 16 to 27, 16 to 28, 16 to 29, 16 to 30, 17 to 18, 17 to 19, 17 to 20, 17 to 21, 17 to 22, 17 to 23, 17 to 24, 17 to 25, 17 to 26, 17 to 27, 17 to 28, 17 to 29, 17 to 30, 18 to 19, 18 to 20, 18 to 21, 18 to 22, 18 to 23, 18 to 24, 18 to 25, 18 to 26, 18 to 27, 18 to 28, 18 to 29, 18 to 30, 19 to 20, 19 to 21, 19 to 22, 19 to 23, 19 to 24, 19 to 25, 19 to 26, 19 to 27, 19 to 28, 19 to 29, 19 to 30, 20 to 21, 20 to 22, 20 to 23, 20 to 24, 20 to 25, 20 to 26, 20 to 27, 20 to 28, 20 to 29, 20 to 30, 21 to 22, 21 to 23, 21 to 24, 21 to 25, 21 to 26, 21 to 27, 21 to 28, 21 to 29, 21 to 30, 22 to 23, 22 to 24, 22 to 25, 22 to 26, 22 to 27, 22 to 28, 22 to 29, 22 to 30, 23 to 24, 23 to 25, 23 to 26, 23 to 27, 23 to 28, 23 to 29, 23 to 30, 24 to 25, 24 to 26, 24 to 27, 24 to 28, 24 to 29, 24 to 30, 25 to 26, 25 to 27, 25 to 28, 25 to 29, 25 to 30, 26 to 27, 26 to 28, 26 to 29, 26 to 30, 27 to 28, 27 to 29, 27 to 30, 28 to 29, 28 to 30, or 29 to 30 linked nucleosides.

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

D. Certain Modified Oligonucleotides

In certain embodiments, the above modifications (sugar, nucleobase, internucleoside linkage) are incorporated into a modified oligonucleotide. In certain embodiments, modified oligonucleotides are characterized by their modification motifs and overall lengths. In certain embodiments, such parameters are each independent of one another. Thus, unless otherwise indicated, each internucleoside linkage of an oligonucleotide having a gapmer sugar motif may be modified or unmodified and may or may not follow the gapmer modification pattern of the sugar modifications. For

example, the internucleoside linkages within the wing regions of a sugar gapmer may be the same or different from one another and may be the same or different from the internucleoside linkages of the gap region of the sugar motif. Likewise, such sugar gapmer oligonucleotides may comprise one or more modified nucleobase independent of the gapmer pattern of the sugar modifications. Unless otherwise indicated, all modifications are independent of nucleobase sequence.

E. Certain Populations of Modified Oligonucleotides

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

F. Nucleobase Sequence

In certain embodiments, oligonucleotides (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.

5 **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.

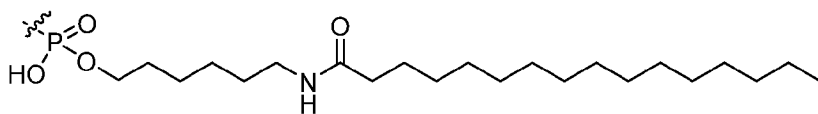
10 In certain embodiments, conjugation of one or more carbohydrate moieties to a modified oligonucleotide can optimize one or more properties of the modified oligonucleotide. In certain embodiments, the carbohydrate moiety is attached to a modified subunit of the modified oligonucleotide. For example,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

20 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 palmitoyl 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).

35 In certain embodiments, conjugate groups may be selected from any of a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

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

In certain embodiments, a conjugate group is a lipid having the following structure:



1. Conjugate Moieties

Conjugate moieties include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates (e.g., GalNAc), antibodies, vitamin moieties, polyethylene glycols, thioethers, polyethers, 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 pyrrolidine.

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 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 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 (AHX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl or substituted or unsubstituted C₂-C₁₀ alkynyl, wherein a nonlimiting list of preferred substituent groups includes hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl.

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

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

In certain embodiments, it is desirable for a conjugate group to be cleaved from the oligonucleotide. For example, in certain circumstances oligomeric compounds comprising a particular conjugate moiety are better taken up by a particular cell type, but once the oligomeric compound has been taken up, it is desirable that the conjugate group be cleaved to release the unconjugated or parent oligonucleotide. Thus, certain conjugate linkers may comprise one or more cleavable moieties. In certain embodiments, a cleavable moiety is a cleavable bond. In certain embodiments, a cleavable

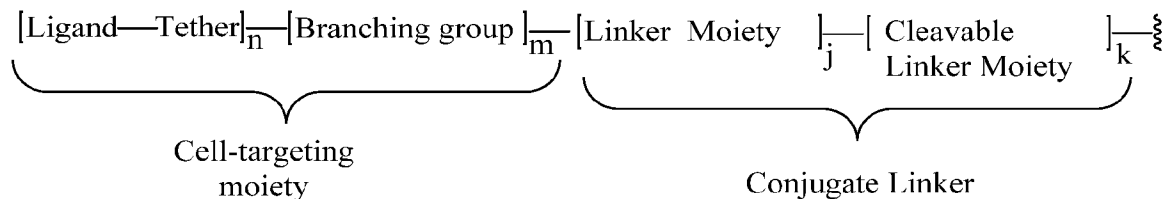
moiety is a group of atoms comprising at least one cleavable bond. In certain embodiments, a cleavable moiety comprises a group of atoms having one, two, three, four, or more than four cleavable bonds. In certain embodiments, a cleavable moiety is selectively cleaved inside a cell or subcellular compartment, such as a lysosome. In certain embodiments, a cleavable moiety is selectively cleaved by endogenous enzymes, such as nucleases.

In certain embodiments, a cleavable bond is selected from among an amide, an ester, an ether, one or both esters of a phosphodiester, a phosphate ester, a carbamate, or a disulfide. In certain embodiments, a cleavable bond is one or both of the esters of a phosphodiester. In certain embodiments, a cleavable moiety comprises a phosphate or phosphodiester. In certain embodiments, the cleavable moiety is a phosphate linkage between an oligonucleotide and a conjugate moiety or conjugate group.

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

3. Cell-Targeting Moieties

In certain embodiments, a conjugate group comprises a cell-targeting moiety. In certain embodiments, a conjugate group has the general formula:



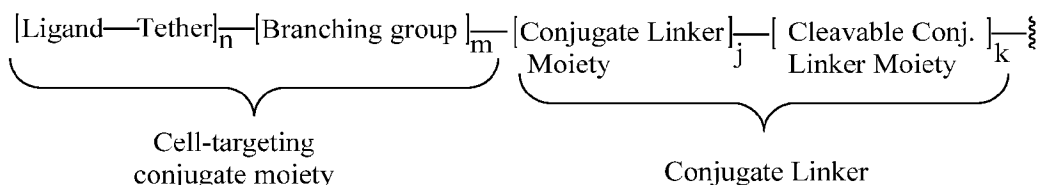
wherein n is from 1 to about 3, m is 0 when n is 1, m is 1 when n is 2 or greater, j is 1 or 0, and k is 1 or 0.

In certain embodiments, n is 1, j is 1 and k is 0. In certain embodiments, n is 1, j is 0 and k is 1. In certain embodiments, n is 1, j is 1 and k is 1. In certain embodiments, n is 2, j is 1 and k is 0. In certain embodiments, n is 2, j is 0 and k is 1. In certain embodiments, n is 2, j is 1 and k is 1. In certain embodiments, n is 3, j is 1 and k is 0. In certain embodiments, n is 3, j is 0 and k is 1. In certain embodiments, n is 3, j is 1 and k is 1.

In certain embodiments, conjugate groups comprise cell-targeting moieties that have at least one tethered ligand. In certain embodiments, cell-targeting moieties comprise two tethered ligands covalently attached to a branching group. In certain embodiments, cell-targeting moieties comprise three tethered ligands covalently attached to a branching group.

In certain embodiments, each ligand of a cell-targeting moiety has an affinity for at least one type of receptor on a target cell. In certain embodiments, each ligand has an affinity for at least one type of receptor on the surface of a mammalian liver cell. In certain embodiments, each ligand has an affinity for the hepatic asialoglycoprotein receptor (ASGP-R). In certain embodiments, each ligand is a carbohydrate.

In certain embodiments, a conjugate group comprises a cell-targeting conjugate moiety. In certain embodiments, a conjugate group has the general formula:



wherein n is from 1 to about 3, m is 0 when n is 1, m is 1 when n is 2 or greater, j is 1 or 0, and k is 1 or 0.

In certain embodiments, n is 1, j is 1 and k is 0. In certain embodiments, n is 1, j is 0 and k is 1. In certain embodiments, n is 1, j is 1 and k is 1. In certain embodiments, n is 2, j is 1 and k is 0. In certain embodiments, n is 2, j is 0 and k is 1. In certain embodiments, n is 2, j is 1 and k is 1. In certain embodiments, n is 3, j is 1 and k is 0. In certain embodiments, n is 3, j is 0 and k is 1. In certain embodiments, n is 3, j is 1 and k is 1.

In certain embodiments, conjugate groups comprise cell-targeting moieties that have at least one tethered ligand. In certain embodiments, cell-targeting moieties comprise two tethered ligands covalently attached to a branching group. In certain embodiments, cell-targeting moieties comprise three tethered ligands covalently attached to a branching group.

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

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

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

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

B. Certain Terminal Groups

In certain embodiments, oligomeric compounds comprise one or more terminal groups. In certain such embodiments, oligomeric compounds comprise a stabilized 5'-phosphate. Stabilized 5'-phosphates include, but are not

limited to 5'-phosphonates, including, but not limited to 5'-vinylphosphonates. In certain embodiments, terminal groups comprise one or more abasic sugar moieties and/or inverted nucleosides. In certain embodiments, terminal groups comprise one or more 2'-linked nucleosides or sugar moieties. In certain such embodiments, the 2'-linked group is an abasic sugar moiety.

III. 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 *in vitro* assay. In certain embodiments, antisense compounds selectively affect one or more target nucleic acid. Such antisense compounds comprise a nucleobase sequence that hybridizes to one or more target nucleic acid, resulting in one or more desired antisense activity and does not hybridize to one or more non-target nucleic acid or does not hybridize to one or more non-target nucleic acid in such a way that results in significant undesired antisense activity.

In certain antisense activities, hybridization of an antisense compound to a target nucleic acid results in 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 agents. RNAi agents may be double-stranded (siRNA or dsRNAi) or single-stranded (ssRNAi).

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

IV. Certain Target Nucleic Acids

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a region that is complementary to a target nucleic acid. In certain embodiments, the target nucleic acid is an endogenous RNA molecule. In certain embodiments, the target nucleic acid encodes a protein. In certain such embodiments, the target

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

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

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

It is possible to introduce mismatch bases without eliminating activity. For example, Gautschi et al (*J. Natl. Cancer Inst.* 93:463-471, March 2001) demonstrated the ability of an oligonucleotide having 100% complementarity to the bcl-2 mRNA and having 3 mismatches to the bcl-xL mRNA to reduce the expression of both bcl-2 and bcl-xL *in vitro* and *in vivo*. Furthermore, this oligonucleotide demonstrated potent anti-tumor activity *in vivo*. Maher and Dolnick
 20 (*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.

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

In certain embodiments, a mismatch is specifically positioned within an oligonucleotide having a gapmer motif.
 30 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. ATN1

35 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 ATN1. In each of the embodiments described above, the oligomeric compounds target the ATN1 nucleic acid. In certain embodiments, the ATN1 nucleic acid has the sequence set forth in SEQ ID NO: 1 (GenBank Accession No. NC_000012.12 truncated from nucleosides

6923463 to 6943321) or SEQ ID NO: 2 (GenBank Accession No. NM_001940.3). In certain embodiments, contacting a cell with an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 reduces the amount of ATN1 RNA, and in certain embodiments reduces the amount of atrophin-1 protein. In certain embodiments, contacting a cell with an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 results in reduced aggregation of atrophin-1 protein. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide and a conjugate group.

In certain embodiments, contacting a cell with an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 reduces the amount of ATN1 RNA in a cell. In certain embodiments, contacting a cell with an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 reduces the amount of atrophin-1 protein in the cell. In certain embodiments, the cell is *in vitro*. In certain embodiments, the cell is in a subject. In certain embodiments, the oligomeric compound consists of a modified oligonucleotide. In certain embodiments, contacting a cell in a subject with an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 ameliorates one or more symptoms or hallmarks of a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the polyglutamine (polyQ) disease or disorder associated with ATN1 is dentatorubral-pallidolysian atrophy (DRPLA).

In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of ATN1 RNA *in vitro* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vitro* assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of ATN1 RNA *in vivo* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vivo* assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of atrophin-1 protein *in vitro* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vitro* assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of atrophin-1 protein *in vivo* by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90% when administered according to the standard *in vivo* assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of ATN1 RNA in the cell of a subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1 or SEQ ID NO: 2 is capable of reducing the amount of atrophin-1 protein or the amount of atrophin-1 protein aggregation in the cell of a subject by at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%.

C. Certain Target Nucleic Acids in Certain Tissues

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 include the cortex, spinal cord, globus pallidus, subthalamic nucleus, thalamus, inferior olive, substantia nigra, and the cerebellum. In certain embodiments, the cells are brain cells. In certain embodiments, the cells include neurons and oligodendrocytes.

V. Certain Methods and Uses

Certain embodiments provided herein relate to methods of reducing or inhibiting ATN1 expression or activity, which can be useful for treating, preventing, or ameliorating a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the polyglutamine (polyQ) disease or disorder associated with ATN1 is dentatorubral-pallidoluysian atrophy (DRPLA).

In certain embodiments, a method comprises administering to a subject an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to an ATN1 nucleic acid. In certain embodiments, the subject has or is at risk for developing a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the subject has or is at risk for developing DRPLA. In certain embodiments, the subject has DRPLA.

In certain embodiments, a method for treating a polyglutamine (polyQ) disease or disorder associated with ATN1 comprises administering to a subject an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to an ATN1 nucleic acid. In certain embodiments, the subject has or is at risk for developing a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the subject has or is at risk for developing DRPLA. In certain embodiments, the subject has DRPLA. In certain embodiments, at least one symptom or hallmark of the polyglutamine (polyQ) disease or disorder associated with ATN1 is ameliorated. In certain embodiments, the at least one symptom or hallmark is seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysidiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

In certain embodiments, a method of reducing expression of ATN1, for example RNA, or reducing the expression of atrophin-1 protein in a cell comprises contacting the cell with an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to an ATN1 nucleic acid. In certain embodiments, the subject has or is at risk for developing a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the subject has or is at risk for developing DRPLA. In certain embodiments, the subject has DRPLA. In certain embodiments, the cell is a neuron or oligodendrocyte. In certain embodiments, the cell is a human cell.

Certain embodiments are drawn to an oligomeric compound, a modified oligonucleotide, an oligomeric duplex, or an antisense agent, any of which having a nucleobase sequence complementary to an ATN1 nucleic acid, for use in treating a polyglutamine (polyQ) disease or disorder associated with ATN1 or for use in the manufacture of a medicament for treating a polyglutamine (polyQ) disease or disorder associated with ATN1. In certain embodiments, the polyglutamine (polyQ) disease or disorder associated with ATN1 is DRPLA.

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

VI. Certain Pharmaceutical Compositions

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 ("artificial CSF" or "aCSF"). In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

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

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

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

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

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

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

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

In certain embodiments, pharmaceutical compositions comprise a delivery system. Examples of delivery systems include, but are not limited to, liposomes and emulsions. Certain delivery systems are useful for preparing certain pharmaceutical compositions including those comprising hydrophobic compounds. In certain embodiments, certain organic solvents such as dimethylsulfoxide are used.

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

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

In certain embodiments, pharmaceutical compositions are prepared for oral administration. In certain embodiments, pharmaceutical compositions are prepared for buccal administration. In certain embodiments, a pharmaceutical composition is prepared for administration by injection (e.g., intravenous, subcutaneous, intramuscular, intrathecal (IT), intracerebroventricular (ICV), etc.). In certain of such embodiments, a pharmaceutical composition comprises a carrier and is formulated in aqueous solution, such as water or physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. In certain embodiments, other ingredients are included (e.g., ingredients that aid in solubility or serve as preservatives). In certain embodiments, injectable suspensions are prepared using appropriate liquid carriers, suspending agents and the like. Certain pharmaceutical compositions for injection are presented in unit dosage form, e.g., in ampoules or in multi-dose containers. Certain pharmaceutical

compositions for injection are suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Certain solvents suitable for use in pharmaceutical compositions for injection include, but are not limited to, lipophilic solvents and fatty oils, such as sesame oil, synthetic fatty acid esters, such as ethyl oleate or triglycerides, and liposomes.

Under certain conditions, certain compounds disclosed herein act as acids. Although such compounds may be drawn or described in protonated (free acid) form or ionized and in association with a cation (salt) form, aqueous solutions of such compounds exist in equilibrium among such forms. For example, a phosphodiester linkage of an oligonucleotide in aqueous solution exists in equilibrium among free acid, anion and salt forms. Unless otherwise indicated, compounds described herein are intended to include all such forms. Moreover, certain oligonucleotides have several such linkages, each of which is in equilibrium. Thus, oligonucleotides in solution exist in an ensemble of forms at multiple positions all at equilibrium. The term "oligonucleotide" is intended to include all such forms. Drawn structures necessarily depict a single form. Nevertheless, unless otherwise indicated, such drawings are likewise intended to include corresponding forms. Herein, a structure depicting the free acid of a compound followed by the term "or a pharmaceutically acceptable salt thereof" expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with a cation or a combination of cations. In certain embodiments, one or more specific cation is identified. The cations include, but are not limited to, sodium, potassium, calcium, and magnesium. In certain embodiments, a structure depicting the free acid of a compound followed by the term "or a pharmaceutically acceptable salt thereof" expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with one or more cations selected from sodium, potassium, calcium, and magnesium.

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

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

In certain embodiments, where a modified oligonucleotide or an oligomeric compound is in solution comprising sodium (e.g., saline), the modified oligonucleotide or oligomeric compound may be partially or fully de-protonated and in association with sodium ions. However, the mass of the protons is nevertheless counted toward the weight of the dose, and the mass of the sodium ions is not counted toward the weight of the dose. Thus, for example, a dose, or dosage unit, of 10 mg of Compound No. 541106 or Compound No. 613801 equals the number of fully protonated molecules that weighs 10 mg. This would be equivalent to 10.58 mg of solvent-free, sodium acetate-free, anhydrous sodiated Compound No. 541106 or 10.61 mg of solvent-free, sodium acetate-free, anhydrous sodiated Compound No. 613801.

In certain embodiments, where a modified oligonucleotide or oligomeric compound is in a solution, such as aCSF, comprising sodium, potassium, calcium, and magnesium, the modified oligonucleotide or oligomeric compound

may be partially or fully de-protonated and in association with sodium, potassium, calcium, and/or magnesium. However, the mass of the protons is nevertheless counted toward the weight of the dose, and the mass of the sodium, potassium, calcium, and magnesium ions is not counted toward the weight of the dose.

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

VII. Certain Hotspot Regions

1. Nucleobases 6584-6607 of SEQ ID NO: 1

In certain embodiments, nucleobases 6584-6607 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 6584-6607 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 528, 2437, 2296, 483, and 2137 are complementary within nucleobases 6584-6607 of SEQ ID NO: 1.

Compounds 1475694, 1441013, 1572931, 1441008, and 1572877 are complementary within nucleobases 6584-6607 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 6584-6607 of SEQ ID NO: 1 achieve at least 66% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 6584-6607 of SEQ ID NO: 1 achieve an average of 76% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

2. Nucleobases 6865-6890 of SEQ ID NO: 1

In certain embodiments, nucleobases 6865-6890 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 6865-6890 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') ccccccdddddddddccccc, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "c" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssssooss or soossssssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 1329, 1241, 1166, 459, 70, and 1116 are complementary within nucleobases 6865-6890 of SEQ ID NO: 1.

Compounds 1573191, 1572821, 1572876, 1143640, 1143641, 1573580, and 1573333 are complementary within nucleobases 6865-6890 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 6865-6890 of SEQ ID NO: 1 achieve at least 38% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 6865-6890 of SEQ ID NO: 1 achieve an average of 63% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

3. Nucleobases 7364-7409 of SEQ ID NO: 1

In certain embodiments, nucleobases 7364-7409 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 7364-7409 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeddccccccccdeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 770, 699, 2100, 2027, 677, 1942, 606, 527, 841, 1799, 769, 716, 654, 605, 492, 876, 1719, and 799 are complementary within nucleobases 7364-7409 of SEQ ID NO: 1.

Compounds 1475422, 1475429, 1573520, 1573522, 1475751, 1573392, 1475699, 1475689, 1475384, 1573610, 1475420, 1475514, 1475584, 1475697, 1475446, 1475608, 1573351, and 1475597 are complementary within nucleobases 7364-7409 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 7364-7409 of SEQ ID NO: 1 achieve at least 61% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 7364-7409 of SEQ ID NO: 1 achieve an average of 81% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

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4. Nucleobases 7405-7430 of SEQ ID NO: 1

In certain embodiments, nucleobases 7405-7430 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 7405-7430 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

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In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

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In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssoos or soossssssssoos, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

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The nucleobase sequences of SEQ ID NOs: 1626, 1557, 1486, 1412, 1337, 1251, and 1187 are complementary within nucleobases 7405-7430 of SEQ ID NO: 1.

Compounds 1573038, 1573460, 1573206, 1573262, 1573360, 1573017, and 1573359 are complementary within nucleobases 7405-7430 of SEQ ID NO: 1.

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In certain embodiments, modified oligonucleotides complementary within nucleobases 7405-7430 of SEQ ID NO: 1 achieve at least 46% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 7405-7430 of SEQ ID NO: 1 achieve an average of 63% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

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5. Nucleobases 7484-7514 of SEQ ID NO: 1

In certain embodiments, nucleobases 7484-7514 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 7484-7514 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

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In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester (“o”) and phosphorothioate (“s”) internucleoside linkages are arranged in order from 5’ to 3’. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5’ to 3’) sosossssssssooss or
 5 soossssssssooss, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 948, 651, 2410, 2316, 2205, 2163, 2073, 2003, 1961, 1872, and 1782 are complementary within nucleobases 7484-7514 of SEQ ID NO: 1.

Compounds 1573130, 1475561, 1573665, 1573327, 1572525, 1573282, 1573001, 1572893, 1573757, 1573403,
 10 and 1573229 are complementary within nucleobases 7484-7514 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 7484-7514 of SEQ ID NO: 1 achieve at least 47% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 7484-7514 of SEQ ID NO: 1 achieve an average of 61% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

6. Nucleobases 7621-7658 of SEQ ID NO: 1

In certain embodiments, nucleobases 7621-7658 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 7621-7658 of SEQ ID NO: 1. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified
 20 oligonucleotides are gapmers.

In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5’ to 3’) eeeeeeeeeeeeeee, wherein each “d” represents a 2’-β-D-deoxyribosyl sugar moiety, and each “e” represents a 2’-
 25 MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester (“o”) and phosphorothioate (“s”) internucleoside linkages are arranged in order from 5’ to 3’. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5’ to 3’) sosossssssssooss or
 30 soossssssssooss, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 2200, 2155, 583, 2434, 2115, 2028, 1914, 1888, 1747, 1693, 1659, 1532, 1493, 1367, 1346, 1262, 1172, 460, and 71 are complementary within nucleobases 7621-7658 of SEQ ID NO: 1.

Compounds 1572397, 1573194, 1475582, 1441010, 1573756, 1573548, 1572721, 1573773, 1572556, 1572896, 1573748, 1572705, 1573497, 1572429, 1573530, 1573145, 1573117, 1143646, and 1143647 are complementary within
 35 nucleobases 7621-7658 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 7621-7658 of SEQ ID NO: 1 achieve at least 27% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 7621-7658 of SEQ ID NO: 1 achieve an average of 61% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

7. Nucleobases 7886-7922 of SEQ ID NO: 1

In certain embodiments, nucleobases 7886-7922 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 7886-7922 of SEQ ID NO: 1. In certain
 5 embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (From 5' to 3')
 10 eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o")
 and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or
 15 soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 1632, 1587, 1452, 1434, 1301, 1260, 1140, 1095, 1021, 960, 2362, 2306, 2224, and 2160 are complementary within nucleobases 7886-7922 of SEQ ID NO: 1.

Compounds 1573116, 1573853, 1572520, 1573721, 1572671, 1573121, 1572371, 1573029, 1573120, 1573331,
 20 1572738, 1573071, 1572911, and 1573261 are complementary within nucleobases 7886-7922 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 7886-7922 of SEQ ID NO: 1 achieve at least 16% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain
 embodiments, modified oligonucleotides complementary within nucleobases 7886-7922 of SEQ ID NO: 1 achieve an average of 57% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

8. Nucleobases 8763-8809 of SEQ ID NO: 1

In certain embodiments, nucleobases 8763-8809 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 8763-8809 of SEQ ID NO: 1. In certain
 30 embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

In certain embodiments, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3')
 eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o")
 and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or

sooooooooooooo, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 1711, 1635, 1524, 1502, 1385, 1296, 1276, 150, 228, 1093, 985, 907, 306, and 2278 are complementary within nucleobases 8763-8809 of SEQ ID NO: 1.

Compounds 1573213, 1573235, 1572498, 1573645, 1572794, 1572543, 1573563, 1143654, 1475477, 1143655, 1572990, 1572331, 1572362, 1143656, 1572728, and 1572533 are complementary within nucleobases 8763-8809 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 8763-8809 of SEQ ID NO: 1 achieve at least 48% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 8763-8809 of SEQ ID NO: 1 achieve an average of 69% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

9. Nucleobases 9082-9107 of SEQ ID NO: 1

In certain embodiments, nucleobases 9082-9107 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 9082-9107 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each “d” represents a 2'-β-D-deoxyribose sugar moiety, and each “e” represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester (“o”) and phosphorothioate (“s”) internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosoooooooooooo or sooooooooooooo, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 1970, 1896, 765, 694, 1801, 643, and 590 are complementary within nucleobases 9082-9107 of SEQ ID NO: 1.

Compounds 1572457, 1572383, 1475415, 1475398, 1573621, 1475507, and 1475594 are complementary within nucleobases 9082-9107 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 9082-9107 of SEQ ID NO: 1 achieve at least 36% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 9082-9107 of SEQ ID NO: 1 achieve an average of 75% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

10. Nucleobases 9093-9174 of SEQ ID NO: 1

In certain embodiments, nucleobases 9093-9174 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 9093-9174 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3')
 5 eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments,
 10 modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 867, 812, 464, 1288, 704, 1215, 75, 1191, 153, 231, 562, 548, 1060, 861, 834, 1029, 690, 680, 309, and 387 are complementary within nucleobases 9093-9174 of SEQ ID NO: 1.

15 Compounds 1475569, 1475687, 1143670, 1572392, 1475456, 1572391, 1143671, 1573399, 1143672, 1143673, 1475632, 1475425, 1475810, 1572349, 1475536, 1475816, 1573225, 1475375, 1475770, 1143674, 1143675, and 1475605 are complementary within nucleobases 9093-9174 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 9093-9174 of SEQ ID NO: 1 achieve at least 36% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In
 20 certain embodiments, modified oligonucleotides complementary within nucleobases 9093-9174 of SEQ ID NO: 1 achieve an average of 68% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

11. Nucleobases 9483-9525 of SEQ ID NO: 1

In certain embodiments, nucleobases 9483-9525 of SEQ ID NO: 1 comprise a hotspot region. In certain
 25 embodiments, modified oligonucleotides are complementary within nucleobases 9483-9525 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3')
 30 eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments,
 35 modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 625, 1359, 1244, 2440, 1150, 1091, 1032, 929, 2413, 2300, and 2259 are complementary within nucleobases 9483-9525 of SEQ ID NO: 1.

Compounds 1475370, 1573767, 1572847, 1441016, 1572584, 1572960, 1573296, 1572736, 1573764, 1573019, and 1573649 are complementary within nucleobases 9483-9525 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 9483-9525 of SEQ ID NO: 1 achieve at least 47% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain
5 embodiments, modified oligonucleotides complementary within nucleobases 9483-9525 of SEQ ID NO: 1 achieve an average of 64% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

12. Nucleobases 10163-10200 of SEQ ID NO: 1

In certain embodiments, nucleobases 10163-10200 of SEQ ID NO: 1 comprise a hotspot region. In certain
10 embodiments, modified oligonucleotides are complementary within nucleobases 10163-10200 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3')
15 eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments,
20 modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 634, 581, 543, 863, 809, 721, 669, 157, and 235 are complementary within nucleobases 10163-10200 of SEQ ID NO: 1.

Compounds 1475440, 1475557, 1475779, 1475546, 1475682, 1475574, 1475678, 1143696, and 1143697 are
25 complementary within nucleobases 10163-10200 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 10163-10200 of SEQ ID NO: 1 achieve at least 57% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 10163-10200 of SEQ ID NO: 1
30 achieve an average of 75% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

13. Nucleobases 11033-11081 of SEQ ID NO: 1

In certain embodiments, nucleobases 11033-11081 of SEQ ID NO: 1 comprise a hotspot region. In certain
35 embodiments, modified oligonucleotides are complementary within nucleobases 11033-11081 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3')

eeeeeddddddddeeeee, wherein each “d” represents a 2’-β-D-deoxyribosyl sugar moiety, and each “e” represents a 2’-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester (“o”) and phosphorothioate (“s”) internucleoside linkages are arranged in order from 5’ to 3’. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5’ to 3’) sosossssssssooss or soossssssssooss, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 94, 172, 681, 250, 502, 927, 878, 792, 732, 328, 406, 2355, 573, 538, 2272, 902, 827, and 740 are complementary within nucleobases 11033-11081 of SEQ ID NO: 1.

Compounds 1143318, 1143319, 1475577, 1475775, 1143320, 1475601, 1475510, 1572717, 1475620, 1475532, 1475658, 1143321, 1143322, 1475459, 1572612, 1475509, 1475750, 1510556, 1475777, 1475763, and 1475695 are complementary within nucleobases 11033-11081 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 11033-11081 of SEQ ID NO: 1 achieve at least 41% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 11033-11081 of SEQ ID NO: 1 achieve an average of 69% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

14. Nucleobases 12214-12244 of SEQ ID NO: 1

In certain embodiments, nucleobases 12214-12244 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 12214-12244 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5’ to 3’) eeeeeeddddddddeeeee, wherein each “d” represents a 2’-β-D-deoxyribosyl sugar moiety, and each “e” represents a 2’-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester (“o”) and phosphorothioate (“s”) internucleoside linkages are arranged in order from 5’ to 3’. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5’ to 3’) sosossssssssooss or soossssssssooss, wherein each “s” represents a phosphorothioate internucleoside linkage and each “o” represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 779, 741, 2370, 645, 2309, 594, 499, 903, 775, and 738 are complementary within nucleobases 12214-12244 of SEQ ID NO: 1.

Compounds 1475449, 1475706, 1572867, 1475517, 1573094, 1475628, 1475496, 1475799, 1475434, and 1475683 are complementary within nucleobases 12214-12244 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 12214-12244 of SEQ ID NO: 1 achieve at least 61% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

In certain embodiments, modified oligonucleotides complementary within nucleobases 12214-12244 of SEQ ID NO: 1 achieve an average of 79% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

15. Nucleobases 12360-12400 of SEQ ID NO: 1

In certain embodiments, nucleobases 12360-12400 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 12360-12400 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') 5'-eeeeeddddddddeeeee-3', wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 2053, 2032, 1925, 1821, 1780, 1696, 1613, 176, 254, 332, 1499, 410, 21, 99, 518, 177, and 255 are complementary within nucleobases 12360-12400 of SEQ ID NO: 1.

Compounds 1572582, 1573643, 1573089, 1572448, 1573158, 1572929, 1572768, 1143343, 1143344, 1143345, 1573383, 1573613, 1143346, 1573315, 1143347, 1573617, 1143348, 1475619, 1143349, and 1143350 are complementary within nucleobases 12360-12400 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 12360-12400 of SEQ ID NO: 1 achieve at least 60% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 12360-12400 of SEQ ID NO: 1 achieve an average of 76% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

16. Nucleobases 12929-12957 of SEQ ID NO: 1

In certain embodiments, nucleobases 12929-12957 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 12929-12957 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeddddddddeeeee, wherein each "d" represents a 2'-β-D-deoxyribsyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o")

and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 2110, 181, 1993, 259, 337, 1847, 1746, 711, and 415 are complementary within nucleobases 12929-12957 of SEQ ID NO: 1.

Compounds 1573672, 1143373, 1572732, 1143374, 1475801, 1143375, 1475433, 1572975, 1572508, 1475491, and 1143376 are complementary within nucleobases 12929-12957 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 12929-12957 of SEQ ID NO: 1 achieve at least 71% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 12929-12957 of SEQ ID NO: 1 achieve an average of 84% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

17. Nucleobases 13300-13330 of SEQ ID NO: 1

In certain embodiments, nucleobases 13300-13330 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 13300-13330 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 2283, 2198, 2139, 2062, 1981, 1909, 1860, 416, 1695, 1622, and 1567 are complementary within nucleobases 13300-13330 of SEQ ID NO: 1.

Compounds 1572645, 1572352, 1572889, 1572778, 1572581, 1572555, 1573174, 1143382, 1573462, 1572923, 1572972, and 1573537 are complementary within nucleobases 13300-13330 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 13300-13330 of SEQ ID NO: 1 achieve at least 73% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 13300-13330 of SEQ ID NO: 1 achieve an average of 87% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

18. Nucleobases 14061-14097 of SEQ ID NO: 1

In certain embodiments, nucleobases 14061-14097 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 14061-14097 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeddddddddeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 1553, 34, 1480, 112, 1331, 190, 1165, 1075, 1059, 982, 2365, 2299, 2243, 2157, 2097, 1982, 1943, and 1858 are complementary within nucleobases 14061-14097 of SEQ ID NO: 1.

Compounds 1573378, 1143425, 1475639, 1573132, 1143426, 1572741, 1573277, 1143427, 1573659, 1572819, 1572623, 1573855, 1573831, 1572814, 1573012, 1573295, 1573216, 1573434, 1572583, 1573426, and 1573156 are complementary within nucleobases 14061-14097 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 14061-14097 of SEQ ID NO: 1 achieve at least 29% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5. In certain embodiments, modified oligonucleotides complementary within nucleobases 14061-14097 of SEQ ID NO: 1 achieve an average of 58% reduction of ATN1 RNA in the standard *in vitro* assay as described in Example 5.

19. Nucleobases 18284-18363 of SEQ ID NO: 1

In certain embodiments, nucleobases 18284-18363 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 18284-18363 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeddddddddeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssooss or soossssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 584, 551, 887, 800, 702, 637, 591, 201, 279, 494, 357, 435, 865, 46, 124, 202, 280, and 358 are complementary within nucleobases 18284-18363 of SEQ ID NO: 1.

Compounds 1475583, 1475821, 1475677, 1475600, 1475450, 1475476, 1475598, 1143493, 1143494, 1475448, 1143495, 1143496, 1475560, 1143497, 1143498, 1143499, 1143500, and 1143501 are complementary within nucleobases 18284-18363 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 18284-18363 of SEQ ID NO: 1 achieve at least 43% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 18284-18363 of SEQ ID NO: 1 achieve an average of 63% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

20. Nucleobases 18658-18689 of SEQ ID NO: 1

In certain embodiments, nucleobases 18658-18689 of SEQ ID NO: 1 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 18658-18689 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, modified oligonucleotides are MOE gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is (from 5' to 3') eeeeeeeeeeeeeee, wherein each "d" represents a 2'-β-D-deoxyribose sugar moiety, and each "e" represents a 2'-MOE sugar moiety.

In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3'. In certain embodiments, modified oligonucleotides have an internucleoside linkage motif of (from 5' to 3') sosossssssssoos or soossssssssoos, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID NOs: 895, 764, 691, 678, 438, 49, 874, 828, 754, 127, 205, and 561 are complementary within nucleobases 18658-18689 of SEQ ID NO: 1.

Compounds 1475739, 1475406, 1475389, 1475752, 1143514, 1475644, 1143515, 1475692, 1475599, 1475767, 1475776, 1143516, 1475442, 1143517, and 1475412 are complementary within nucleobases 18658-18689 of SEQ ID NO: 1.

In certain embodiments, modified oligonucleotides complementary within nucleobases 18658-18689 of SEQ ID NO: 1 achieve at least 37% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4. In certain embodiments, modified oligonucleotides complementary within nucleobases 18658-18689 of SEQ ID NO: 1 achieve an average of 59% reduction of ATN1 RNA in the standard *in vitro* assay as described in Examples 1 and 4.

21. Additional Hotspot Regions

In certain embodiments, the nucleobase ranges described in the Table below comprise hotspot regions. Each hotspot region begins with the nucleobase of SEQ ID NO: 1 identified in the "Start Site SEQ ID NO: 1" column and ends with the nucleobase of SEQ ID NO: 1 identified in the "Stop Site SEQ ID NO: 1" column. In certain embodiments,

oligomeric compounds comprise modified oligonucleotides that are complementary within any of the hotspot regions 1-26, as defined in the table below. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are 5-10-5 MOE gapmers. In certain embodiments, the sugar motif for the gapmers is 5'- eeeeeeddddddddeeeee -3'; wherein each "d" represents a 2'-β-D-deoxyribosyl sugar moiety, and each "e" represents a 2'-MOE sugar moiety. In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged as: 5'- sosossssssssssooss - 3' or 5'- soossssssssssooss - 3', wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequence of compounds listed in the "Compound No. in range" column in the table below are complementary to SEQ ID NO: 1 within the specified hotspot region. The nucleobase sequence of the oligonucleotides listed in the "SEQ ID NOs in range" column in the table below are complementary to SEQ ID NO: 1 within the specified hotspot region.

The nucleobase sequences of the oligomeric compounds in the table below are complementary to SEQ ID NO: 1 within the specified hotspot region. In certain embodiments, compounds comprising a modified oligonucleotide complementary to nucleobases within the hotspot region achieve at least "Min.% Red." (minimum % reduction, relative to untreated control cells) of ATN1 RNA in the standard *in vitro* assay, as indicated in the table below. In certain embodiments, modified oligonucleotides complementary to nucleobases within the hotspot region achieve an average of "Avg.% Red." (average % reduction, relative to untreated control cells) of ATN1 RNA in the standard *in vitro* assay, as indicated in the table below. In certain embodiments, modified oligonucleotides complementary to nucleobases within the hotspot region achieve a maximum "Max. % Red. " (maximum % reduction, relative to untreated control cells) of ATN1 RNA in the standard *in vitro* assay, as indicated in the table below.

Table 1. ATN1 Hotspots

Hotspot ID	Start Site SEQ ID NO: 1	Stop Site SEQ ID NO: 1	Min. % Red. In vitro	Max. % Red. In vitro	Avg % Red. In vitro	Compound No. in range	SEQ ID NOs in range
1	5742	5766	29	89	58	1475572, 1475715, 1573653, 1572587, 1572468	870, 819, 1278, 1151, 1066
2	7457	7479	64	72	68	1573620, 1573317, 1475744, 1143644	1205, 1114, 748, 304
3	7672	7726	56	92	68	1572903, 1573679, 1572367, 1572535, 1573740, 1143648, 1572875, 1143649	1771, 1732, 1595, 1526, 1508, 149, 1390, 227, 1248

						1572534, 1572937	
4	7773	7804	83	95	87	1573223, 1573595, 1573734	2085, 2030, 1959
5	7911	7932	79	85	82	1573669, 1572677, 1572464	1730, 1611, 1520
6	8906	8945	61	86	77	1475693, 1475651, 1475676, 1475542, 1475399, 1143666	739, 665, 604, 509, 844, 152
7	8948	8982	53	85	65	1572603, 1572825, 1572544, 1572395, 1573364, 1573068, 1572952	1457, 1387, 1297, 1216, 1188, 1097, 1016
8	9047	9089	39	93	66	1572691, 1475505, 1475798, 1573444, 1143668, 1143669, 1573172, 1475377, 1475787, 1475547, 1475813	2284, 787, 757, 2250, 308, 386, 2153, 627, 615, 510, 905
9	9168	9191	72	93	83	1572344, 1143676, 1572861, 1573321, 1572539, 1573608	2197, 465, 2091, 1976, 1953
10	9700	9723	68	93	83	1475803, 1475631, 1475661, 1475635, 1475708	833, 729, 666, 597, 530
11	10477	10526	34	71	61	1475386, 1475761, 1475633, 1475691, 1475796, 1510542, 1475361, 1475747	629, 613, 519, 890, 832, 1212, 689, 676
12	10711	10744	49	75	61	1475655, 1475498, 1475650, 1475749, 1475550, 1475368, 1475439	807, 713, 664, 612, 511, 836, 777

13	10807	10839	62	83	74	1475488, 1475783, 1475385, 1510482, 1475563	709, 683, 557, 983, 512
14	12406	12428	62	82	72	1573798, 1143352, 1573207, 1143353, 1143354	1286, 411, 22, 100
15	12459	12487	44	69	56	1573002, 1572699, 1573324, 1572518, 1475529, 1475765, 1573771, 1573442, 1572591, 1572551	2074, 1992, 1939, 1825, 791, 752, 1809, 1722, 1607, 1528
16	12471	12496	51	81	67	1475473, 1475735, 1475526, 1572476, 1475703, 1475535, 1475611	569, 537, 858, 1369, 816, 717, 659
17	12689	12714	68	95	85	1573260, 1572916, 1573362, 1572840, 1143368, 1573535, 1572710, 1572713	1109, 1014, 962, 2368, 258, 2212, 2130
18	12731	12751	88	96	92	1572945, 1572560	2071, 1977
19	13151	13184	52	84	75	1143379, 1573077, 1572356, 1573532, 1572709, 1572552, 1572496	182, 1703, 1592, 1565, 1462, 1371, 1292
20	13532	13555	58	69	63	1572857, 1573584, 1573134, 1572594, 1573377	1245, 1200, 1101, 996, 964
21	13545	13567	80	90	85	1573735, 1573486, 1573291, 1573792	2114, 2024, 1938, 1889
22	14053	14076	54	74	62	1572836, 1572443, 1475774, 1573550, 1143422	1839, 1742, 614, 1727, 267

23	15154	15202	42	80	66	1475376, 1475481, 1143459, 1143460, 1475814, 1143461	839, 785, 351, 429, 761, 40
24	15188	15217	54	84	70	1573088, 1573704, 1143462, 1572681, 1143463, 1572789, 1572988, 1573603, 1573128, 1573056	1853, 1802, 118, 1682, 196, 1537, 1498, 1407, 1321
25	15349	15376	52	77	61	1475760, 1475667, 1475818, 1475482	679, 601, 549, 853
26	18527	18557	60	88	72	1475795, 1475769, 1572651, 1573668, 1572439, 1573818, 1143507, 1573287, 1572950, 1143508	547, 899, 2358, 2335, 2202, 2189, 359, 2004, 437

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

Although the sequence listing accompanying this filing identifies each sequence as either “RNA” or “DNA” as
10 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 an uracil of RNA). Accordingly, nucleic acid
15 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^mCGAUCG,” wherein ^mC 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 ¹H hydrogen atoms. Isotopic substitutions encompassed by the compounds herein include but are not limited to: ²H or ³H in place of ¹H, ¹³C or ¹⁴C in place of ¹²C, ¹⁵N in place of ¹⁴N, ¹⁷O or ¹⁸O in place of ¹⁶O, and ³³S, ³⁴S, ³⁵S, or ³⁶S in place of ³²S. 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 complementary to human ATN1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to a human ATN1 RNA were designed and tested for their single dose effects on ATN1 RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in Table 2 below are 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein “e” represents a 2'-MOE ribosyl sugar moiety, and each “d” represents a 2'-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sosossssssssooss; wherein each “s” represents a phosphorothioate internucleoside linkage, and each “o” represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

“Start site” indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. “Stop site” indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in Table 2 below is 100% complementary to SEQ ID NO: 1 (GenBank Accession No. NC_000012.12 truncated from nucleosides 6923463 to 6943321), to SEQ ID NO: 2 (GenBank Accession No. NM_001940.3), or to both. ‘N/A’ indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured A431 cells were treated with modified oligonucleotide at a concentration of 4,000 nM by free uptake at a density of 10,000 cells per well. After a treatment period of 48 hours, total RNA was isolated from the cells and ATN1 RNA levels were measured by quantitative real-time RT-PCR. ATN1 RNA levels were measured by human primer-probe set RTS40640 (forward sequence AGGAGACCAATGCACCAA, designated herein as SEQ ID NO: 3; reverse sequence GCTTCGGTTGTCCTGGTC, designated herein as SEQ ID NO: 4; and probe sequence CCGAGGGAGTTCCTGCTCAGTTT, designated herein as SEQ ID NO: 5). ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA relative to the amount of ATN1 RNA in untreated control cells (% UTC). The values marked with a “†” indicate that the modified oligonucleotide is complementary to the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of the modified oligonucleotides complementary to the amplicon region.

Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled “AID”.

Table 2

Reduction of ATN1 RNA by 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages in A-431 cells

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATN1 RNA (% UTC)	AID	SEQ ID NO
1143311	4882	4901	28	47	TGGCTGGCTCCGAGCGGGAT	45	A	15
1143317	10769	10788	313	332	GGAGGCCCGGCCCTCGATC	87	A	16
1143323	12097	12116	522	541	TCGGAGGGAGACTGTGGCCG	16†	A	17
1143329	12119	12138	544	563	CCGCCCCGTCCAAGCTATCCA	4†	A	18
1143335	12129	12148	554	573	CATTAAGGCTCCGCCCGTCC	6†	A	19
1143341	12164	12183	589	608	CTGGTCGATATCCCTAGGGT	9†	A	20
1143347	12377	12396	802	821	GGGAGCATGATATCCAGTGG	12	A	21
1143353	12408	12427	833	852	CCTGGAACATTCGAGATGTG	38	A	22
1143359	12538	12557	963	982	TTACCCCCATTAGGGCCCCC	107	A	23
1143365	12589	12608	1014	1033	CTAGCCCCAGAGCTTGATAC	36	A	24
1143371	12812	12831	1237	1256	AAGTCCACCCATACCCTGTC	61	A	25
1143377	13142	13161	1567	1586	TAAGAGGCGGCCATAGGGAG	66	A	26
1143383	13313	13332	1738	1757	GGGCCCAGAGTTTCCGTGAT	82	A	27
1143389	13365	13384	1790	1809	CGTGGTGGGAGCTACCGCCC	87	A	28
1143395	13624	13643	2049	2068	GTAGCCGAAGAGGTGGTGAC	68	A	29

1143401	13642	13661	2067	2086	GCAATGACCGTGGAAAGGGT	21	A	30
1143407	13715	13734	2140	2159	GGCTCTCTTTCCGTACGGTG	25	A	31
1143413	13818	13837	2243	2262	GCGAGGTTCTCGATAGCCC	44	A	32
1143419	13857	13876	2282	2301	TGGGCGAGCCCCGGCTTGAAG	97	A	33
1143425	14062	14081	2487	2506	TGGCTGGGTACATCTACCAC	42	A	34
1143431	14424	14443	2566	2585	CACGAAGTACAGGTCGCTGC	61	A	35
1143437	14512	14531	2654	2673	TTTCTTCGCGCGCGCGCTGC	110	A	36
1143443	15031	15050	2760	2779	TCCACCGGAGCACGGCCCTC	91	A	37
1143449	15078	15097	2807	2826	CCGGTTCAAATGGAGGGCGA	106	A	38
1143455	15100	15119	2829	2848	GGCACTGTAGCCACCGCACT	95	A	39
1143461	15183	15202	2912	2931	TGCGATTGCCAGGAGACATG	36	A	40
1143467	15247	15266	2976	2995	GCCGGGACATTGTAACCCAG	86	A	41
1143473	15301	15320	3030	3049	CGTTCACGGGCTTCCCGTTC	78	A	42
1143479	15396	15415	3125	3144	GAAAGGGATCCAAGCCCGGC	87	A	43
1143485	15689	15708	3418	3437	GATAGCATCTTGCTGGTGCA	101	A	44
1143491	18070	18089	3747	3766	TAGTAGTCCTCCTGGGCAGG	106	A	45
1143497	18319	18338	3804	3823	TGCTCTCTTGATCGCAGGTT	32	A	46
1143503	18426	18445	3911	3930	TGCGGAGGCCCTGCAACTGA	94	A	47
1143509	18539	18558	4024	4043	GGTCCAAGATTCTGTGCGCT	53	A	48
1143515	18663	18682	4148	4167	GCTACGCAAAACAGCCACAT	26	A	49
1143521	1055	1074	N/A	N/A	TTCGCAGAAGCAGAGCGGGA	114	A	50
1143527	1130	1149	N/A	N/A	CCCTACCCATACAGAACTAG	106	A	51
1143533	1497	1516	N/A	N/A	TGTAACCCAATCCAACCCCG	128	A	52
1143539	1504	1523	N/A	N/A	AGCTAGCTGTAACCCAATCC	93	A	53
1143545	2137	2156	N/A	N/A	CTGAAGTCCCTTGAATTGGT	86	A	54
1143551	2551	2570	N/A	N/A	CCACCAAGCGGCAACATCTC	119	A	55
1143557	2791	2810	N/A	N/A	AAGCAGTCGGGTGAAGACTG	107	A	56
1143563	4418	4437	N/A	N/A	AAGCCGCGGTCCCTCCGAAA	49	A	57
1143569	4565	4584	N/A	N/A	CCTCGGCGCGGTTCCGACCC	26	A	58
1143575	4695	4714	N/A	N/A	CCGGAGCAAACCCCGATCCC	67	A	59
1143581	4924	4943	N/A	N/A	CCAGGCGGCCGAGACCTTA	88	A	60
1143587	5210	5229	N/A	N/A	TGAGTCTGCGGGTCCCGGAT	53	A	61
1143593	5286	5305	N/A	N/A	TGCCTTCGCCCCGAACCCCA	82	A	62
1143599	5458	5477	N/A	N/A	GGTTCATCAGCCACAATCCC	52	A	63
1143605	5655	5674	N/A	N/A	GATAACCCACACTACTGGGC	86	A	64
1143611	5836	5855	N/A	N/A	CCTATATAGATCACAGCTCC	63	A	65
1143617	5913	5932	N/A	N/A	TGAAGGTACCTACCCTAGTC	80	A	66
1143623	6042	6061	N/A	N/A	CTACCATAGCAACACAGTGG	93	A	67
1143629	6092	6111	N/A	N/A	CCAATAAACATTCTGAAGCCC	99	A	68
1143635	6735	6754	N/A	N/A	CTTCTGAGAATCCGGGACCT	73	A	69
1143641	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	9	A	70
1143647	7639	7658	N/A	N/A	ACAGCAATCATAGTATGCCC	21	A	71
1143653	8721	8740	N/A	N/A	CACGGAACCATACTGATGCA	51	A	72

1143659	8836	8855	N/A	N/A	CAGACTAAGCTTACCCATGT	84	A	73
1143665	8895	8914	N/A	N/A	ACCCACTAACATCAGTAGGT	69	A	74
1143671	9110	9129	N/A	N/A	CCAATCCATCCGTATCTGTC	24	A	75
1143677	9193	9212	N/A	N/A	TCCGTGAGCAAACAACACAG	56	A	76
1143683	9330	9349	N/A	N/A	GACTAAACCTAGGTAGCCCC	52	A	77
1143689	10124	10143	N/A	N/A	GATGTACCTACAAGCCCCAA	53	A	78
1143695	10139	10158	N/A	N/A	AGGGCAGAAAATTCGGATGT	66	A	79
1143701	10207	10226	N/A	N/A	TGGGCTACCTTAGCTATCTA	126	A	80
1143707	10562	10581	N/A	N/A	CTCATTTTAACTCACCGAGT	134	A	81
1143713	10933	10952	N/A	N/A	CACCGTTACCTCTGCCAAA	85	A	82
1143719	11121	11140	N/A	N/A	AGGATGGCGACAAGGGTTTC	95	A	83
1143725	11358	11377	N/A	N/A	TCCTCCGACTAAGACTTCTC	63	A	84
1143731	11949	11968	N/A	N/A	GAGTACTCTTGCTCAAGCCC	120	A	85
1143737	14180	14199	N/A	N/A	ACTACACCAGCGCAAGGCCC	37	A	86
1143743	14732	14751	N/A	N/A	CAGTGGTACCTCCCTCCGA	99	A	87
1143749	14852	14871	N/A	N/A	GCTCCCGAATATTTGCCCTT	89	A	88
1143755	14878	14897	N/A	N/A	CCACCTGGAACCTAACTGCG	91	A	89
1143761	16480	16499	N/A	N/A	ATTATCGCCTATGACACCCA	87	A	90
1143767	17733	17752	N/A	N/A	TCGAACCTCTTAGGCTGACA	49	A	91
1143773	17862	17881	N/A	N/A	CCAACGGATAACAAGTACCT	85	A	92
1143312	4903	4922	49	68	CTGCTGGTAGCTCGGGACGG	67	B	93
1143318	11033	11052	426	445	CGACCCTGCTTGTTGACCTT	50	B	94
1143324	12098	12117	523	542	ATCGGAGGGGAGACTGTGGCC	14†	B	95
1143330	12124	12143	549	568	AGGCTCCGCCCGTCCAAGCT	3†	B	96
1143336	12135	12154	560	579	CATCATCATTAAGGCTCCGC	38†	B	97
1143342	12333	12352	758	777	AGCTAGCCTCTGGCTGTCTGA	51	B	98
1143348	12378	12397	803	822	TGGGAGCATGATATCCAGTG	34	B	99
1143354	12409	12428	834	853	GCCTGGAACATTTCGAGATGT	29	B	100
1143360	12540	12559	965	984	GCTTACCCCCATTAGGGCCC	72	B	101
1143366	12591	12610	1016	1035	CACTAGCCCCAGAGCTTGAT	89	B	102
1143372	12817	12836	1242	1261	GGAGGAAGTCCACCCATACC	65	B	103
1143378	13143	13162	1568	1587	CTAAGAGGCGGCCATAGGGA	24	B	104
1143384	13354	13373	1779	1798	CTACCGCCCTCCAGTGGGTG	32	B	105
1143390	13604	13623	2029	2048	CGTAGGCACCGGTGGGAAAG	77	B	106
1143396	13627	13646	2052	2071	AGGGTAGCCGAAGAGGTGGT	49	B	107
1143402	13645	13664	2070	2089	GTGGCAATGACCGTGGAAG	62	B	108
1143408	13745	13764	2170	2189	GGTGGCTGTCTTGTAAGCCC	95	B	109
1143414	13819	13838	2244	2263	GGCGAGGTTCTCGATAGCC	61	B	110
1143420	13861	13880	2286	2305	ACGGTGGGCGAGCCCGGCTT	72	B	111
1143426	14064	14083	2489	2508	CATGGCTGGGTACATCTACC	24	B	112
1143432	14466	14485	2608	2627	CAGGTCGGCCCGCTTCTTGG	62	B	113
1143438	14514	14533	2656	2675	CTTTTCTTCGCGCGCGCT	102	B	114
1143444	15038	15057	2767	2786	TGGGCATTCCACCGGAGCAC	68	B	115

1143450	15085	15104	2814	2833	GCACTGCCCCGGTTCAAATGG	89	B	116
1143456	15141	15160	2870	2889	TGAGAGTGCGCAAGGCTGGA	67	B	117
1143462	15191	15210	2920	2939	TGGATGGTTGCGATTGCCAG	34	B	118
1143468	15248	15267	2977	2996	GGCCGGGACATTGTAACCCA	69	B	119
1143474	15322	15341	3051	3070	TTGAGGCGGTCACGGAGGTC	72	B	120
1143480	15471	15490	3200	3219	GCCCCAGGCTCGGATGAAAG	73	B	121
1143486	15692	15711	3421	3440	ATGGATAGCATCTTGCTGGT	50	B	122
1143492	18073	18092	3750	3769	CTGTAGTAGTCCTCTGGGC	92	B	123
1143498	18340	18359	3825	3844	GGTCCAATGTAGGAGCCATG	52	B	124
1143504	18428	18447	3913	3932	GCTGCGGAGGCCCTGCAACT	90	B	125
1143510	18540	18559	4025	4044	TGGTCCAAGATTCTGTGCGC	73	B	126
1143516	18667	18686	4152	4171	CGATGCTACGCAAAACAGCC	42	B	127
1143522	1058	1077	N/A	N/A	ACCTTCGAGAAGCAGAGCG	115	B	128
1143528	1133	1152	N/A	N/A	GGGCCCTACCCATACAGAAC	86	B	129
1143534	1498	1517	N/A	N/A	CTGTAACCCAATCCAACCCC	103	B	130
1143540	1569	1588	N/A	N/A	CCCATTTGGTCTCCAGGCAAC	96	B	131
1143546	2291	2310	N/A	N/A	TGGAGCAGCTCAGTAGATTT	98	B	132
1143552	2620	2639	N/A	N/A	CCCGGCCGTGAAGCCAGCAC	59	B	133
1143558	2815	2834	N/A	N/A	CTAAAGATCCCCTGGGTCAC	92	B	134
1143564	4422	4441	N/A	N/A	CCCGAAGCCGCGTCCCTCC	25	B	135
1143570	4566	4585	N/A	N/A	CCCTCGGCGCGGTTCCGACC	76	B	136
1143576	4697	4716	N/A	N/A	CCCCGGAGCAAACCCCGATC	76	B	137
1143582	4949	4968	N/A	N/A	GGACAGAACCCCGCGGGCCC	79	B	138
1143588	5214	5233	N/A	N/A	CTTTTGAGTCTGCGGGTCCC	78	B	139
1143594	5292	5311	N/A	N/A	CCATTCTGCCTTCGCCCCGA	78	B	140
1143600	5523	5542	N/A	N/A	CGCTGGAAAACCTCCGGCTC	85	B	141
1143606	5659	5678	N/A	N/A	TTGGGATAACCCACACTACT	66	B	142
1143612	5837	5856	N/A	N/A	CCCTATATAGATCACAGCTC	75	B	143
1143618	5916	5935	N/A	N/A	GCTTGAAGGTACCTACCCTA	31	B	144
1143624	6049	6068	N/A	N/A	TGGATCACTACCATAGCAAC	70	B	145
1143630	6723	6742	N/A	N/A	CGGGACCTTCAGAGAGGCCT	97	B	146
1143636	6765	6784	N/A	N/A	ACCAGCAGATAACGATGCAC	79	B	147
1143642	6903	6922	N/A	N/A	TACAGTGGAGTCACAAGCTC	84	B	148
1143648	7704	7723	N/A	N/A	TCACCAAGTCAGTTAGGTTA	41	B	149
1143654	8784	8803	N/A	N/A	ACGGCATGTCCATATTCTGT	21	B	150
1143660	8840	8859	N/A	N/A	GGAACAGACTAAGCTTACCC	29	B	151
1143666	8926	8945	N/A	N/A	TGTGTGCGCTCTTCTTGTA	35	B	152
1143672	9113	9132	N/A	N/A	CAGCCAATCCATCCGTATCT	32	B	153
1143678	9264	9283	N/A	N/A	CTAGTACTTGAGCTCCCTAA	45	B	154
1143684	9334	9353	N/A	N/A	CCAAGACTAAACCTAGGTAG	56	B	155
1143690	10125	10144	N/A	N/A	GGATGTACCTACAAGCCCCA	57	B	156
1143696	10172	10191	N/A	N/A	CTGCTCGAAGTATAATCTCT	34	B	157
1143702	10208	10227	N/A	N/A	ATGGGCTACCTTAGCTATCT	65	B	158

1143708	10583	10602	N/A	N/A	CGCCCCTCATCTTTCATGTC	67	B	159
1143714	10934	10953	N/A	N/A	CCACCGTTACCCTCTGCCAA	78	B	160
1143720	11122	11141	N/A	N/A	CAGGATGGCGACAAGGGTTT	83	B	161
1143726	11720	11739	N/A	N/A	TTTATACCACTTCTGGCCGG	93	B	162
1143732	11950	11969	N/A	N/A	TGAGTACTCTTGCTCAAGCC	86	B	163
1143738	14187	14206	N/A	N/A	CTAAACACTACACCAGCGC	47	B	164
1143744	14733	14752	N/A	N/A	GCAGTGGTACCTCCCCTCCG	65	B	165
1143750	14863	14882	N/A	N/A	CTGCGGCCCGCTCCCGAA	98	B	166
1143756	14925	14944	N/A	N/A	GTTTCGACAGCCGAATGCCA	58	B	167
1143762	16483	16502	N/A	N/A	CTCATTATCGCCTATGACAC	85	B	168
1143768	17737	17756	N/A	N/A	GGATTCTGAACCTCTTAGGCT	51	B	169
1143774	17870	17889	N/A	N/A	GCATATGACCAACGGATAAC	90	B	170
1143313	10754	10773	298	317	CGATCTCAGTTCTTCCCGGG	94	C	171
1143319	11034	11053	427	446	CCGACCCTGCTTGTTGACCT	59	C	172
1143325	12106	12125	531	550	CTATCCAGATCGGAGGGAGA	45†	C	173
1143331	12125	12144	550	569	AAGGCTCCGCCCGTCCAAGC	4†	C	174
1143337	12136	12155	561	580	CCATCATCATTAAAGGCTCCG	19†	C	175
1143343	12372	12391	797	816	CATGATATCCAGTGGGTGTC	21	C	176
1143349	12380	12399	805	824	CATGGGAGCATGATATCCAG	29	C	177
1143355	12531	12550	956	975	CATTAGGGCCCCCCTGAT	70	C	178
1143361	12541	12560	966	985	TGCTTACCCCATTAGGGCC	80	C	179
1143367	12619	12638	1044	1063	GTGGTAGGCGGCTTTGTTGG	19	C	180
1143373	12931	12950	1356	1375	GAGCTACTACTAGAGGATGA	22	C	181
1143379	13151	13170	1576	1595	GCTGTTGGCTAAGAGGCGGC	10	C	182
1143385	13356	13375	1781	1800	AGCTACCGCCCTCCAGTGGG	63	C	183
1143391	13605	13624	2030	2049	CCGTAGGCACCGGTGGGAAA	76	C	184
1143397	13628	13647	2053	2072	AAGGGTAGCCGAAGAGGTGG	61	C	185
1143403	13648	13667	2073	2092	ACGGTGGCAATGACCGTGGA	65	C	186
1143409	13769	13788	2194	2213	CGACCCGGGTTTGTATCCGG	93	C	187
1143415	13820	13839	2245	2264	TGGCGAGGTTCTTCGATAGC	65	C	188
1143421	13865	13884	2290	2309	TCCCACGGTGGGCGAGCCCG	70	C	189
1143427	14066	14085	2491	2510	GGCATGGCTGGGTACATCTA	16	C	190
1143433	14493	14512	2635	2654	CTCGGCCTCGCGCCGCACCT	95	C	191
1143439	14524	14543	2666	2685	GCTCGCGCTCCTTTTCTTCG	54	C	192
1143445	15040	15059	2769	2788	GATGGGCATTCCACCGGAGC	61	C	193
1143451	15086	15105	2815	2834	CGCACTGCCCCGGTTCAAATG	91	C	194
1143457	15149	15168	2878	2897	ATATTCACTGAGAGTGCGCA	62	C	195
1143463	15193	15212	2922	2941	AATGGATGGTTGCGATTGCC	20	C	196
1143469	15265	15284	2994	3013	GGATCACTGCTGTACAGGGC	33	C	197
1143475	15326	15345	3055	3074	AGGCTTGAGGCGGTACGGA	37	C	198
1143481	15534	15553	3263	3282	CATAGGACATGTCAGGCCGC	83	C	199
1143487	15694	15713	3423	3442	GCATGGATAGCATCTTGCTG	60	C	200
1143493	18297	18316	3782	3801	ACAGTGGCTTGTCGCTTTCC	45	C	201

1143499	18342	18361	3827	3846	AAGGTCCAATGTAGGAGCCA	42	C	202
1143505	18440	18459	3925	3944	ACTCTCTGTCCAGCTGCGGA	87	C	203
1143511	18541	18560	4026	4045	CTGGTCCAAGATTCTGTGCG	42	C	204
1143517	18668	18687	4153	4172	ACGATGCTACGCAAAACAGC	28	C	205
1143523	1066	1085	N/A	N/A	AGGACCAGACCTTCGCAGAA	103	C	206
1143529	1134	1153	N/A	N/A	TGGGCCCTACCCATACAGAA	55	C	207
1143535	1499	1518	N/A	N/A	GCTGTAACCCAATCCAACCC	78	C	208
1143541	1820	1839	N/A	N/A	TGGGCTACAATGGATACTAA	107	C	209
1143547	2418	2437	N/A	N/A	CCCTCAGTAGAGCTCCAGAT	91	C	210
1143553	2634	2653	N/A	N/A	GCAGTCAGTCTGCTCCCGGC	82	C	211
1143559	2935	2954	N/A	N/A	TGCTGGCAAGCTCATGGGTA	73	C	212
1143565	4425	4444	N/A	N/A	CTCCCCGAAGCCGCGGTCCC	73	C	213
1143571	4567	4586	N/A	N/A	GCCCTCGGCGCGGTTCCGAC	57	C	214
1143577	4699	4718	N/A	N/A	GCCCCCGGAGCAAACCCCGA	87	C	215
1143583	5136	5155	N/A	N/A	CGATCCTCCCGAAACCCTGG	74	C	216
1143589	5238	5257	N/A	N/A	AACCCCGGCCTCGATGTTCC	22	C	217
1143595	5296	5315	N/A	N/A	CTATCCATTCTGCCTTCGCC	52	C	218
1143601	5524	5543	N/A	N/A	ACGCTGGAAAACCTCCGGCT	99	C	219
1143607	5762	5781	N/A	N/A	CCTGGAGTGCCTGTAAGGTT	68	C	220
1143613	5844	5863	N/A	N/A	AAGGCCTCCCTATATAGATC	86	C	221
1143619	5940	5959	N/A	N/A	TCCTATAGCACCTCAGGTAA	35	C	222
1143625	6051	6070	N/A	N/A	ACTGGATCACTACCATAGCA	74	C	223
1143631	6724	6743	N/A	N/A	CCGGGACCTTCAGAGAGGCC	100	C	224
1143637	6816	6835	N/A	N/A	CCAGACTAACAACCCAGTCC	85	C	225
1143643	7438	7457	N/A	N/A	GCAGGCAATCACTGTAATA	36	C	226
1143649	7706	7725	N/A	N/A	GTTACCAAGTCAGTTAGGT	9	C	227
1143655	8785	8804	N/A	N/A	AACGGCATGTCCATATTCTG	19	C	228
1143661	8844	8863	N/A	N/A	AGTGGGAACAGACTAAGCTT	70	C	229
1143667	9018	9037	N/A	N/A	GCTAAGTGTCAAGTCCCTCC	29	C	230
1143673	9114	9133	N/A	N/A	ACAGCCAATCCATCCGTATC	64	C	231
1143679	9266	9285	N/A	N/A	CTCTAGTACTTGAGCTCCCT	46	C	232
1143685	9533	9552	N/A	N/A	AATCAAACCCATGTCGGTGA	108	C	233
1143691	10126	10145	N/A	N/A	CGGATGTACCTACAAGCCCC	92	C	234
1143697	10181	10200	N/A	N/A	AGGCAGATTCTGCTCGAAGT	15	C	235
1143703	10258	10277	N/A	N/A	GCCTTTGGGCCAAGAGGTAC	84	C	236
1143709	10649	10668	N/A	N/A	ACCTAACTTTATGGTGCACA	97	C	237
1143715	10941	10960	N/A	N/A	CCGAGCTCCACCGTTACCCT	104	C	238
1143721	11352	11371	N/A	N/A	GACTAAGACTTCTCACCCAG	96	C	239
1143727	11721	11740	N/A	N/A	TTTTATACCACTTCTGGCCG	90	C	240
1143733	11954	11973	N/A	N/A	GTGGTGAGTACTCTTGCTCA	62	C	241
1143739	14282	14301	N/A	N/A	TTGTAGCCCCCGCCTCAAAA	84	C	242
1143745	14766	14785	N/A	N/A	GCTGAAAACCTTTTGGGCTC	60	C	243
1143751	14872	14891	N/A	N/A	GGAACCTTAAGTGGGCCCCC	90	C	244

1143757	14932	14951	N/A	N/A	CCCATTGTGTTTCGACAGCCG	65	C	245
1143763	16490	16509	N/A	N/A	AGTAAAGCTCATTATCGCCT	49	C	246
1143769	17743	17762	N/A	N/A	GAATTGGGATTTCGAACCTCT	44	C	247
1143775	18077	18096	N/A	N/A	GTACCTGTAGTAGTCCTCCT	78	C	248
1143314	10755	10774	299	318	TCGATCTCAGTTCTTCCCGG	46	D	249
1143320	11037	11056	430	449	ACTCCGACCCTGCTTGTTGA	33	D	250
1143326	12114	12133	539	558	CGTCCAAGCTATCCAGATCG	28†	D	251
1143332	12126	12145	551	570	TAAGGCTCCGCCCCGTCCAAG	8†	D	252
1143338	12151	12170	576	595	CTAGGGTCGCTGCTGCCATC	13†	D	253
1143344	12373	12392	798	817	GCATGATATCCAGTGGGTGT	22	D	254
1143350	12381	12400	806	825	CCATGGGAGCATGATATCCA	44	D	255
1143356	12533	12552	958	977	CCCATTAGGGCCCCCACTG	86	D	256
1143362	12542	12561	967	986	CTGCTTACCCCCATTAGGGC	54	D	257
1143368	12693	12712	1118	1137	GAGGCAGGTTTCGGTGTACA	8	D	258
1143374	12933	12952	1358	1377	CAGAGCTACTACTAGAGGAT	29	D	259
1143380	13199	13218	1624	1643	GGTGGACTGGGCCCCAGTAG	81	D	260
1143386	13358	13377	1783	1802	GGAGCTACCGCCCTCCAGTG	92	D	261
1143392	13606	13625	2031	2050	ACCGTAGGCACCGGTGGGAA	84	D	262
1143398	13630	13649	2055	2074	GAAAGGGTAGCCGAAGAGGT	16	D	263
1143404	13649	13668	2074	2093	CACGGTGGCAATGACCGTGG	89	D	264
1143410	13771	13790	2196	2215	GGCGACCCGGGTTTGTATCC	104	D	265
1143416	13821	13840	2246	2265	GTGGCGAGGTTCTCTGATAG	80	D	266
1143422	14057	14076	2482	2501	GGGTACATCTACCACCTTGG	45	D	267
1143428	14411	14430	2553	2572	TCGCTGCGCGCGCACGAGTT	99	D	268
1143434	14496	14515	2638	2657	CTGCTCGGCCTCGCGCCGCA	47	D	269
1143440	14577	14596	2719	2738	TTCAAGCTCGCGCTCCTTCT	44	D	270
1143446	15042	15061	2771	2790	GAGATGGGCATTCCACCGGA	37	D	271
1143452	15087	15106	2816	2835	CCGCACTGCCCCGGTTCAAAT	105	D	272
1143458	15151	15170	2880	2899	GCATATTCACTGAGAGTGCG	66	D	273
1143464	15239	15258	2968	2987	ATTGTAACCCAGGAGCCCCG	6	D	274
1143470	15268	15287	2997	3016	GCTGGATCACTGCTGTACAG	62	D	275
1143476	15331	15350	3060	3079	AAGCCAGGCTTGAGGCGGTC	71	D	276
1143482	15535	15554	3264	3283	GCATAGGACATGTCAGGCCG	81	D	277
1143488	17422	17441	3449	3468	TGAGAGGGTGCACCGAGGCA	54	D	278
1143494	18299	18318	3784	3803	CTACAGTGGCTTGTCGCTTT	41	D	279
1143500	18343	18362	3828	3847	CAAGGTCCAATGTAGGAGCC	29	D	280
1143506	18479	18498	3964	3983	ACATCGGGCCTTGGCCTTCT	39	D	281
1143512	18544	18563	4029	4048	GACCTGGTCCAAGATTCTGT	73	D	282
1143518	18671	18690	4156	4175	CACACGATGCTACGCAAAC	61	D	283
1143524	1069	1088	N/A	N/A	GCCAGGACCAGACCTTCGCA	113	D	284
1143530	1367	1386	N/A	N/A	GTCTGGGAGTTACTAAGGTA	107	D	285
1143536	1500	1519	N/A	N/A	AGCTGTAACCCAATCCAACC	97	D	286
1143542	1824	1843	N/A	N/A	GGAATGGGCTACAATGGATA	96	D	287

1143548	2433	2452	N/A	N/A	AGTGTGGATTAGGAGCCCTC	113	D	288
1143554	2760	2779	N/A	N/A	GACCCAAATCCCTGGGTATC	90	D	289
1143560	4098	4117	N/A	N/A	CTAGCCGTGGCGGAATGTGG	91	D	290
1143566	4506	4525	N/A	N/A	CGATCCCGGGCCCCCTCGGCC	98	D	291
1143572	4569	4588	N/A	N/A	CGGCCCTCGGCGCGGTTCCG	62	D	292
1143578	4704	4723	N/A	N/A	CGCCGGCCCCCGGAGCAAAC	94	D	293
1143584	5140	5159	N/A	N/A	TTCCCGATCCTCCCGAAACC	48	D	294
1143590	5253	5272	N/A	N/A	CCGTTTTCCTCCGCCAACCC	45	D	295
1143596	5368	5387	N/A	N/A	TCCGGAACCCGTGTTCTGGT	99	D	296
1143602	5525	5544	N/A	N/A	CACGCTGGAAAACCTCCGGC	89	D	297
1143608	5772	5791	N/A	N/A	TCGCAACTTGCCTGGAGTGC	60	D	298
1143614	5846	5865	N/A	N/A	CTAAGGCCTCCCTATATAGA	93	D	299
1143620	5941	5960	N/A	N/A	CTCCTATAGCACCTCAGGTA	96	D	300
1143626	6053	6072	N/A	N/A	CCACTGGATCACTACCATAG	97	D	301
1143632	6725	6744	N/A	N/A	TCCGGGACCTTCAGAGAGGC	78	D	302
1143638	6817	6836	N/A	N/A	GCCAGACTAACAACCCAGTC	70	D	303
1143644	7460	7479	N/A	N/A	TTAGCACCAGCCTACACTCC	28	D	304
1143650	7847	7866	N/A	N/A	CCGAAGAACAACCCACCA	32	D	305
1143656	8789	8808	N/A	N/A	GGTAAACGGCATGTCCATAT	12	D	306
1143662	8859	8878	N/A	N/A	AGTGCTGCTAGCTCCAGTGG	57	D	307
1143668	9061	9080	N/A	N/A	CCCTATAGCCAGCTGTATTC	55	D	308
1143674	9145	9164	N/A	N/A	ACTTGGTGTAGACTGGGTTA	33	D	309
1143680	9289	9308	N/A	N/A	GAGAGCCCCATAAAGGACCC	97	D	310
1143686	10042	10061	N/A	N/A	CCACGGAGCCTTACAAAGGA	9	D	311
1143692	10129	10148	N/A	N/A	ATTTCGGATGTACCTACAAGC	52	D	312
1143698	10182	10201	N/A	N/A	GAGGCAGATTCTGCTCGAAG	58	D	313
1143704	10265	10284	N/A	N/A	ACCCTAAGCCTTTGGGCCAA	85	D	314
1143710	10650	10669	N/A	N/A	CACCTAACTTTATGGTGCAC	94	D	315
1143716	10944	10963	N/A	N/A	CTCCCGAGCTCCACCGTTAC	64	D	316
1143722	11353	11372	N/A	N/A	CGACTAAGACTTCTCACCCA	113	D	317
1143728	11857	11876	N/A	N/A	CGCCTGTAAAACCCTATTCC	74	D	318
1143734	11955	11974	N/A	N/A	TGTGGTGAGTACTCTTGCTC	69	D	319
1143740	14327	14346	N/A	N/A	CGAGCTGCCCCGATGGAGCCC	107	D	320
1143746	14767	14786	N/A	N/A	CGCTGAAAACCTTTTGGGCT	93	D	321
1143752	14875	14894	N/A	N/A	CCTGGAACCTTAACTGCGGCC	95	D	322
1143758	14981	15000	N/A	N/A	AGTGGAGTCAAAGCGGCAGT	93	D	323
1143764	16491	16510	N/A	N/A	AAGTAAAGCTCATTATCGCC	71	D	324
1143770	17744	17763	N/A	N/A	GGAATTGGGATTCTGAACCTC	78	D	325
1143776	18080	18099	N/A	N/A	AGGGTACCTGTAGTAGTCCT	74	D	326
1143315	10759	10778	303	322	CCCCTCGATCTCAGTTCTTC	100	E	327
1143321	11048	11067	441	460	GAGATCTCCTCACTCCGACC	35	E	328
1143327	12115	12134	540	559	CCGTCCAAGCTATCCAGATC	14†	E	329
1143333	12127	12146	552	571	TTAAGGCTCCGCCCCGTCCAA	23†	E	330

1143339	12161	12180	586	605	GTCGATATCCCTAGGGTCGC	31†	E	331
1143345	12374	12393	799	818	AGCATGATATCCAGTGGGTG	14	E	332
1143351	12382	12401	807	826	TCCATGGGAGCATGATATCC	55	E	333
1143357	12534	12553	959	978	CCCCATTAGGGCCCCCACT	78	E	334
1143363	12545	12564	970	989	GTGCTGCTTACCCCCATTAG	16	E	335
1143369	12768	12787	1193	1212	GACCAGGTAGTGGTTGGGCC	27	E	336
1143375	12934	12953	1359	1378	GCAGAGCTACTACTAGAGGA	11	E	337
1143381	13200	13219	1625	1644	CGGTGGACTGGGCCCCAGTA	66	E	338
1143387	13363	13382	1788	1807	TGGTGGGAGCTACCGCCCTC	113	E	339
1143393	13609	13628	2034	2053	GTGACCGTAGGCACCGGTGG	61	E	340
1143399	13635	13654	2060	2079	CCGTGGAAAGGGTAGCCGAA	35	E	341
1143405	13675	13694	2100	2119	GTTTTGTAGCCTGCTGGCGA	61	E	342
1143411	13772	13791	2197	2216	AGGCGACCCGGGTTTGTATC	83	E	343
1143417	13853	13872	2278	2297	CGAGCCCGGCTTGAAGGTCC	89	E	344
1143423	14059	14078	2484	2503	CTGGGTACATCTACCACCTT	73	E	345
1143429	14419	14438	2561	2580	AGTACAGGTCGCTGCGCGCG	80	E	346
1143435	14508	14527	2650	2669	TTCGCGCGCGCTGCTCGG	77	E	347
1143441	14579	14598	2721	2740	CGTTC AAGCTCGCGCTCCTT	83	E	348
1143447	15043	15062	2772	2791	AGAGATGGGCATTCACCGG	63	E	349
1143453	15092	15111	2821	2840	AGCCACCGCACTGCCCCGTT	30	E	350
1143459	15159	15178	2888	2907	GAGGCCGGGCATATTCCTG	30	E	351
1143465	15241	15260	2970	2989	ACATTGTAACCCAGGAGCCC	84	E	352
1143471	15296	15315	3025	3044	ACGGGCTTCCCGTTCCCTCT	81	E	353
1143477	15358	15377	3087	3106	GGTTCAGCTCACTAGGCTT	85	E	354
1143483	15537	15556	3266	3285	CAGCATAGGACATGTCAGGC	40	E	355
1143489	17458	17477	3485	3504	TCCGGGTAAGGTGAGACCCT	78	E	356
1143495	18310	18329	3795	3814	GATCGCAGGTTCTACAGTGG	42	E	357
1143501	18344	18363	3829	3848	CCAAGGTCCAATGTAGGAGC	36	E	358
1143507	18536	18555	4021	4040	CCAAGATTCTGTGCGCTTTC	22	E	359
1143513	18634	18653	4119	4138	GAAATAATCACACCAACGGG	52	E	360
1143519	18676	18695	4161	4180	GGTGGCACACGATGCTACGC	87	E	361
1143525	1115	1134	N/A	N/A	ACTAGAACCTATTTTAGCCT	104	E	362
1143531	1393	1412	N/A	N/A	GGCTCAAAGTAGGATAGTCC	88	E	363
1143537	1501	1520	N/A	N/A	TAGCTGTAACCCAATCCAAC	82	E	364
1143543	1921	1940	N/A	N/A	CTGTACCACTCAGTTCAGTC	80	E	365
1143549	2544	2563	N/A	N/A	GCGGCAACATCTCCCAGGAC	69	E	366
1143555	2774	2793	N/A	N/A	CTGGGCTTAATGTGGACCCA	98	E	367
1143561	4156	4175	N/A	N/A	GGAGGCGCAGCGCGAGTTGG	77	E	368
1143567	4507	4526	N/A	N/A	GCGATCCCCGGGCCCCCTCGGC	55	E	369
1143573	4638	4657	N/A	N/A	CCTGGCCGCCCGGAATGCCC	73	E	370
1143579	4762	4781	N/A	N/A	CCGACCCCCCGGAGGGCGG	99	E	371
1143585	5198	5217	N/A	N/A	TCCCGGATACCCTCTGGCCC	84	E	372
1143591	5276	5295	N/A	N/A	CGGAACCCCACTCACAGCAT	77	E	373

1143597	5376	5395	N/A	N/A	CCCCAGGCTCCGGAACCCGT	99	E	374
1143603	5556	5575	N/A	N/A	AACCGTCACAAAGACATGGC	56	E	375
1143609	5774	5793	N/A	N/A	GGTCGCAACTTGCCTGGAGT	60	E	376
1143615	5848	5867	N/A	N/A	AACTAAGGCCTCCCTATATA	35	E	377
1143621	5950	5969	N/A	N/A	ACTCCTACCCTCCTATAGCA	113	E	378
1143627	6080	6099	N/A	N/A	CGAAGCCCCCCCAACCAATC	43	E	379
1143633	6730	6749	N/A	N/A	GAGAATCCGGGACCTTCAGA	69	E	380
1143639	6818	6837	N/A	N/A	TGCCAGACTAACAAACCAGT	58	E	381
1143645	7468	7487	N/A	N/A	GTCATGTTTTAGCACCAGCC	6	E	382
1143651	7848	7867	N/A	N/A	TCCGAAGAACAACACCCACC	61	E	383
1143657	8792	8811	N/A	N/A	CTAGGTAAACGGCATGTCCA	29	E	384
1143663	8893	8912	N/A	N/A	CCACTAACATCAGTAGGTCT	66	E	385
1143669	9063	9082	N/A	N/A	ATCCCTATAGCCAGCTGTAT	61	E	386
1143675	9155	9174	N/A	N/A	CTATCCTCCTACTTGGTGTA	39	E	387
1143681	9320	9339	N/A	N/A	AGGTAGCCCCAAATTGTAGA	28	E	388
1143687	10044	10063	N/A	N/A	TTCCACGGAGCCTTACAAAG	49	E	389
1143693	10136	10155	N/A	N/A	GCAGAAAATTCCGGATGTACC	89	E	390
1143699	10183	10202	N/A	N/A	GGAGGCAGATTCTGCTCGAA	52	E	391
1143705	10277	10296	N/A	N/A	GCAAGCGGCCCAACCCTAAG	101	E	392
1143711	10651	10670	N/A	N/A	GCACCTAACTTTATGGTGCA	98	E	393
1143717	10995	11014	N/A	N/A	TACTCGGGCCTTCTGTTAGA	106	E	394
1143723	11355	11374	N/A	N/A	TCCGACTAAGACTTCTCACC	31	E	395
1143729	11858	11877	N/A	N/A	CCGCCTGTAAAACCCTATTC	87	E	396
1143735	12080	12099	N/A	N/A	CCGAGGGAGTTCCTGCTGTA	5†	E	397
1143741	14601	14620	N/A	N/A	CAGTGACGCACTCACCACGC	92	E	398
1143747	14768	14787	N/A	N/A	TCGCTGAAAACCTTTTGGGC	77	E	399
1143753	14876	14895	N/A	N/A	ACCTGGAACTTAACTGCGGC	46	E	400
1143759	14982	15001	N/A	N/A	AAGTGGAGTCAAAGCGGCAG	117	E	401
1143765	17623	17642	N/A	N/A	AACTAGGCCCATCCCCCAC	73	E	402
1143771	17852	17871	N/A	N/A	ACAAGTACCTGCTCTGGACC	88	E	403
1143777	18083	18102	N/A	N/A	CCTAGGGTACCTGTAGTAGT	83	E	404
1143316	10763	10782	307	326	CCGCCCCCTCGATCTCAGTT	76	F	405
1143322	11049	11068	442	461	TGAGATCTCCTCACTCCGAC	36	F	406
1143328	12116	12135	541	560	CCCGTCCAAGCTATCCAGAT	5†	F	407
1143334	12128	12147	553	572	ATTAAGGCTCCGCCCCGTCCA	21†	F	408
1143340	12163	12182	588	607	TGGTCGATATCCCTAGGGTC	34†	F	409
1143346	12376	12395	801	820	GGAGCATGATATCCAGTGGG	3	F	410
1143352	12407	12426	832	851	CTGGAACATTTCGAGATGTGG	18	F	411
1143358	12535	12554	960	979	CCCCATTAGGGCCCCCCCAC	91	F	412
1143364	12546	12565	971	990	GGTGCTGCTTACCCCCATTA	31	F	413
1143370	12804	12823	1229	1248	CCATACCCTGTCCCATGGCG	56	F	414
1143376	12938	12957	1363	1382	TGCTGCAGAGCTACTACTAG	18	F	415
1143382	13308	13327	1733	1752	CAGAGTTTCCGTGATGCTGC	6	F	416

1143388	13364	13383	1789	1808	GTGGTGGGAGCTACCGCCCT	77	F	417
1143394	13619	13638	2044	2063	CGAAGAGGTGGTGACCGTAG	63	F	418
1143400	13638	13657	2063	2082	TGACCGTGGAAGGGTAGCC	59	F	419
1143406	13714	13733	2139	2158	GCTCTCTTCCGTACGGTGG	35	F	420
1143412	13817	13836	2242	2261	CGAGGTTCTCGATAGCCCG	65	F	421
1143418	13854	13873	2279	2298	GCGAGCCCGGCTTGAAGGTC	17	F	422
1143424	14060	14079	2485	2504	GCTGGGTACATCTACCACCT	49	F	423
1143430	14422	14441	2564	2583	CGAAGTACAGGTGCTGCGC	84	F	424
1143436	14510	14529	2652	2671	TCTTCGCGCGCGCGTGCTC	107	F	425
1143442	15028	15047	2757	2776	ACCGGAGCACGGCCCTCCTG	81	F	426
1143448	15044	15063	2773	2792	CAGAGATGGGCATTCCACCG	67	F	427
1143454	15099	15118	2828	2847	GCACTGTAGCCACCGCACTG	103	F	428
1143460	15162	15181	2891	2910	CATGAGGCCGGGCATATTCA	37	F	429
1143466	15245	15264	2974	2993	CGGGACATTGTAACCCAGGA	82	F	430
1143472	15300	15319	3029	3048	GTTACGGGCTTCCCGTTCC	75	F	431
1143478	15395	15414	3124	3143	AAAGGGATCCAAGCCCGGCC	88	F	432
1143484	15547	15566	3276	3295	GCCAGCCGCTCAGCATAGGA	54	F	433
1143490	17461	17480	3488	3507	GGATCCGGGTAAAGGTGAGAC	78	F	434
1143496	18312	18331	3797	3816	TTGATCGCAGGTTCTACAGT	57	F	435
1143502	18349	18368	3834	3853	GTGCTCCAAGGTCCAATGTA	71	F	436
1143508	18538	18557	4023	4042	GTCCAAGATTCTGTGCGCTT	27	F	437
1143514	18662	18681	4147	4166	CTACGCAAAACAGCCACATC	63	F	438
1143520	1026	1045	N/A	N/A	GGGACAGCCTTGAAGTTCCT	56	F	439
1143526	1126	1145	N/A	N/A	ACCCATACAGAACTAGAACC	104	F	440
1143532	1494	1513	N/A	N/A	AACCCAATCCAACCCCGATA	101	F	441
1143538	1503	1522	N/A	N/A	GCTAGCTGTAACCCAATCCA	114	F	442
1143544	2134	2153	N/A	N/A	AAGTCCCTTGAATTGGTTGG	100	F	443
1143550	2548	2567	N/A	N/A	CCAAGCGGCAACATCTCCA	82	F	444
1143556	2775	2794	N/A	N/A	ACTGGGCTTAATGTGGACCC	91	F	445
1143562	4417	4436	N/A	N/A	AGCCGCGGTCCCTCCGAAAT	82	F	446
1143568	4518	4537	N/A	N/A	CCCGCACCCGCGCATCCCG	62	F	447
1143574	4688	4707	N/A	N/A	AAACCCCGATCCCCGCTCTG	66	F	448
1143580	4917	4936	N/A	N/A	GCCGCAGACCTTACCTGCTG	86	F	449
1143586	5207	5226	N/A	N/A	GTCTGCGGGTCCCGGATACC	51	F	450
1143592	5280	5299	N/A	N/A	CGCCCGGAACCCCACTCACA	8	F	451
1143598	5428	5447	N/A	N/A	TACCACACCCCTTCCCGTT	93	F	452
1143604	5653	5672	N/A	N/A	TAACCCACACTACTGGGCCC	100	F	453
1143610	5835	5854	N/A	N/A	CTATATAGATCACAGCTCCA	62	F	454
1143616	5901	5920	N/A	N/A	CCCTAGTCAAAATAAGCCCA	62	F	455
1143622	6017	6036	N/A	N/A	GGTGCCCTCAAGAGACCAT	96	F	456
1143628	6081	6100	N/A	N/A	TCGAAGCCCCCAACCAAT	75	F	457
1143634	6734	6753	N/A	N/A	TTCTGAGAATCCGGGACCTT	75	F	458
1143640	6869	6888	N/A	N/A	GCAGGCTAAATTTTCAGGATC	32	F	459

1143646	7638	7657	N/A	N/A	CAGCAATCATAGTATGCCCT	39	F	460
1143652	7849	7868	N/A	N/A	ATCCGAAGAACAACACCCAC	88	F	461
1143658	8795	8814	N/A	N/A	CTGCTAGGTAAACGGCATGT	42	F	462
1143664	8894	8913	N/A	N/A	CCCACTAACATCAGTAGGTC	43	F	463
1143670	9101	9120	N/A	N/A	CCGTATCTGTCTATCAGCAG	21	F	464
1143676	9169	9188	N/A	N/A	ACCAGTTTTTAAGCCTATCC	10	F	465
1143682	9322	9341	N/A	N/A	CTAGGTAGCCCCAAATTGTA	73	F	466
1143688	10120	10139	N/A	N/A	TACCTACAAGCCCCAATCCA	55	F	467
1143694	10138	10157	N/A	N/A	GGGCAGAAAATTCGGATGTA	38	F	468
1143700	10205	10224	N/A	N/A	GGCTACCTTAGCTATCTAAA	91	F	469
1143706	10286	10305	N/A	N/A	GAGAACTGAGCAAGCGGCCC	78	F	470
1143712	10842	10861	N/A	N/A	GACAGAATACCTTGGCTGTC	73	F	471
1143718	11117	11136	N/A	N/A	TGGCGACAAGGGTTTCCCAC	91	F	472
1143724	11356	11375	N/A	N/A	CTCCGACTAAGACTTCTCAC	104	F	473
1143730	11875	11894	N/A	N/A	GCAGCCAGTCTTGTTCCTCG	74	F	474
1143736	14178	14197	N/A	N/A	TACACCAGCGCAAGGCCCT	107	F	475
1143742	14731	14750	N/A	N/A	AGTGGTACCTCCCCTCCGAC	92	F	476
1143748	14849	14868	N/A	N/A	CCCGAATATTTGCCCTTCTT	74	F	477
1143754	14877	14896	N/A	N/A	CACCTGGAACCTAACTGCGG	87	F	478
1143760	15931	15950	N/A	N/A	GATACTAGACTATGGAGAGA	40	F	479
1143766	17624	17643	N/A	N/A	CAACTAGGCCCATCCCCCA	101	F	480
1143772	17857	17876	N/A	N/A	GGATAACAAGTACCTGCTCT	91	F	481
1143778	18085	18104	N/A	N/A	ACCCTAGGGTACCTGTAGTA	104	F	482

Example 2: Dose-dependent inhibition of human ATN1 in A431 cells by modified oligonucleotides, *in vitro*

Modified oligonucleotides selected from the example above were tested at various doses in A431 cells. A431 cells plated at a density of 10,000 cells per well were treated using free uptake with various 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 ATN1 RNA levels were measured by quantitative real-time RT-PCR. Human ATN1 primer-probe set RTS40640 (described herein above) was used to measure RNA levels as described above. ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA, relative to the amount of ATN1 RNA in untreated control cells (% UTC).

The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the tables below.

Table 3

Dose-dependent reduction of human ATN1 RNA in A431 cells by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)				IC ₅₀ (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1143346	60	26	10	5	0.11
1143347	71	53	25	17	0.39
1143354	71	54	43	25	0.63
1143378	65	50	33	22	0.36

1143384	109	84	87	76	>6
1143401	86	79	62	58	>6
1143407	79	72	53	44	2.79
1143426	68	52	31	20	0.41
1143515	121	89	64	70	>6
1143564	97	82	66	55	>6
1143569	109	124	103	143	>6
1143618	93	83	63	42	3.81
1143641	83	55	24	11	0.51
1143647	78	68	43	23	0.93
1143649	71	36	18	11	0.25
1143654	101	70	54	39	2.24
1143660	81	60	53	30	1.26
1143671	76	64	45	27	0.97
1143672	103	100	82	54	>6

Table 4

Dose-dependent reduction of human ATN1 RNA in A431 cells by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)				IC ₅₀ (μM)
	94 nM	375 nM	1500 nM	6000 nM	
1143343	112	97	78	52	>6
1143344	97	71	45	25	1.31
1143346	78	32	16	7	0.27
1143367	85	67	49	30	1.35
1143368	48	25	12	7	0.05
1143373	97	67	46	32	1.48
1143379	110	119	108	79	>6
1143398	72	56	29	18	0.47
1143427	68	49	33	24	0.40
1143463	70	39	31	21	0.32
1143464	82	80	79	83	>6
1143517	78	64	59	44	3.25
1143589	107	86	75	59	>6
1143644	110	84	74	55	>6
1143650	117	100	82	59	>6
1143655	82	78	64	43	4.45
1143656	75	50	26	13	0.42
1143686	83	73	59	45	3.81
1143697	90	89	68	54	>6

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Table 5

Dose-dependent reduction of human ATN1 RNA in A431 cells by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)				IC ₅₀ (μM)
	94 nM	375 nM	1500 nM	6000 nM	

1143345	70	46	24	12	0.32
1143346	64	30	15	9	0.15
1143352	81	37	29	15	0.39
1143363	81	60	41	29	0.94
1143369	95	74	44	48	2.52
1143375	81	47	24	12	0.43
1143376	92	67	41	25	1.1
1143382	62	48	26	16	0.26
1143418	95	109	100	86	>6
1143446	111	107	94	79	>6
1143453	92	99	98	110	>6
1143459	74	73	55	50	5.31
1143507	60	42	29	23	0.21
1143592	96	94	88	79	>6
1143645	75	55	30	16	0.49
1143657	97	70	52	34	1.80
1143670	82	51	35	26	0.67
1143676	54	33	20	14	0.10
1143681	90	66	45	35	1.44

Example 3: Dose-dependent inhibition of human ATN1 in fibroblast cells by modified oligonucleotides, *in vitro*

Modified oligonucleotides selected from the examples above were tested at various doses in GM13716

Dentatorubral-Pallidolusian Atrophy (DRPLA) patient fibroblast cells (Coriell Institute). GM13716 cells plated at a density of 17,000 cells per well were treated using electroporation with various concentrations of modified

oligonucleotide as specified in the table below. After a treatment period of approximately 24 hours, total RNA was isolated from the cells and ATN1 RNA levels were measured by quantitative real-time RT-PCR. Human ATN1 primer-probe set RTS40640 (described herein above) was used to measure RNA levels as described above. ATN1 RNA levels were normalized to GAPDH. Human GAPDH was measured using the human primer-probe set RTS104 (forward sequence GAAGGTGAAGGTCGGAGTC, designated herein as SEQ ID NO: 6; reverse sequence

GAAGATGGTGTATGGGATTTC, designated herein as SEQ ID NO: 7; probe sequence

CAAGCTTCCCGTTCTCAGCC, designated herein as SEQ ID NO: 8). Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA, relative to the amount of ATN1 RNA in untreated control cells (% UTC). The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using GraphPad Prism software (v8.2.0, San Diego, CA) using the [inhibitor] vs. normalized response function: $Y = 100/(1+X/IC_{50})$.

Table 6: Dose-dependent reduction of human ATN1 RNA in fibroblasts by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)						IC ₅₀ (μM)
	0.082 nM	0.247 nM	0.741 nM	2.22 nM	6.67 nM	20 nM	
1143346	106	102	89	124	125	113	>0.02
1143347	90	80	51	23	13	4	0.79
1143641	86	97	59	28	13	3	1.11

Example 4: Effect of 5-10-5 MOE gapmers complementary to human ATN1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to a human ATN RNA were designed and tested for their single dose effects on ATN1 RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein "e" represents a 2'-MOE ribosyl sugar moiety, and each "d" represents a 2'-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the table below is 100% complementary to SEQ ID NO: 1 (GenBank Accession No. NC_000012.12 truncated from nucleosides 6923463 to 6943321), to SEQ ID NO: 2 (GenBank Accession No. NM_001940.3), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured A431 cells were treated with modified oligonucleotide at a concentration of 4,000 nM by free uptake at a density of 10,000 cells per well. After a treatment period of 48 hours, total RNA was isolated from the cells and ATN1 RNA levels were measured by quantitative real-time RT-PCR. ATN1 RNA levels were measured by human primer-probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA relative to the amount of ATN1 RNA in untreated control cells (% UTC). The values marked with a "†" indicate that the modified oligonucleotide is complementary to the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of the modified oligonucleotides complementary to the amplicon region. Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 7

Reduction of ATN1 RNA by 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages in A-431 cells

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATN1 RNA (% UTC)	AID	SEQ ID NO
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCC	11	G	483
1475374	11723	11742	N/A	N/A	GTTTTTATACCACTTCTGGC	52	G	484
1475379	8624	8643	N/A	N/A	TATCTTCTGAACCTTCAACT	104	G	485
1475395	10624	10643	N/A	N/A	TGTTCTTCTTCTCTAGACCC	69	G	486
1475397	12589	12608	1014	1033	CTAGCCCCAGAGCTTGATAC	73	G	24
1475400	12129	12148	554	573	CATTAAGGCTCCGCCCGTCC	8†	G	19
1475413	1067	1086	N/A	N/A	CAGGACCAGACCTTCGCAGA	68	G	487
1475419	12479	12498	904	923	GGGTCCAGACAAAACCTCCAC	74	G	488
1475437	15342	15361	3071	3090	GCTTCACCTCAAAGCCAGGC	64	G	489

1475438	12644	12663	1069	1088	AGGTAGGTTCCCACCACCCA	75	G	490
1475444	11113	11132	N/A	N/A	GACAAGGGTTTCCCACCTCA	85†	G	491
1475446	7381	7400	N/A	N/A	TAAGCACATTACCTTCATT	33	G	492
1475447	11913	11932	N/A	N/A	GGATTTCTCACTTTCCTCAC	70	G	493
1475448	18308	18327	3793	3812	TCGCAGGTTCTACAGTGGCT	30	G	494
1475457	14280	14299	N/A	N/A	GTAGCCCCCGCCTCAAAACC	71	G	495
1475466	18217	18236	N/A	N/A	CTCTGACCTTGCCCCCTCTT	99	G	496
1475471	13648	13667	2073	2092	ACGGTGGCAATGACCGTGGA	83	G	186
1475477	8784	8803	N/A	N/A	ACGGCATGTCCATATTCTGT	21	G	150
1475479	17558	17577	N/A	N/A	CAACTTCCATCCTTACCAAA	92	G	497
1475484	7713	7732	N/A	N/A	AGAACCTGTTACCAAGTCA	25	G	498
1475486	10562	10581	N/A	N/A	CTCATTTTAACTCACCGAGT	90	G	81
1475496	12221	12240	646	665	AGAGTCATTCTCCACACTTC	13	G	499
1475497	4919	4938	N/A	N/A	CGGCCGCAGACCTTACCTGC	100	G	500
1475504	14520	14539	2662	2681	GCGCTCCTTTTCTTCGCGCG	102	G	501
1475510	11039	11058	432	451	TCACTCCGACCCTGCTTGTT	17	G	502
1475511	18227	18246	N/A	N/A	TTGAGACCAACTCTGACCTT	79	G	503
1475513	10760	10779	304	323	GCCCCTCGATCTCAGTTCTT	63	G	504
1475522	4690	4709	N/A	N/A	GCAAACCCCGATCCCCGCTC	31	G	505
1475525	7029	7048	N/A	N/A	ACCTTACTTTAAAAAGAAAA	80	G	506
1475527	11076	11095	469	488	TGCATTGGTCTCCTCACTTT	6†	G	507
1475541	10510	10529	201	220	GTGGAGACCCCATCTCCTC	93	G	508
1475542	8910	8929	N/A	N/A	GTGATTGACCTTTAAACCCA	14	G	509
1475547	9069	9088	N/A	N/A	ATCCAAATCCCTATAGCCAG	12	G	510
1475550	10720	10739	264	283	TTCTTCCGTCCACTCCTCAT	46	G	511
1475563	10820	10839	364	383	CCTGGACTTCTCAGCTTTC	38	G	512
1475564	12916	12935	1341	1360	GATGAATAAGGAAACCTCAT	44	G	513
1475565	1856	1875	N/A	N/A	TGAGCTCTTCTCCCTTGTTT	95	G	514
1475567	10709	10728	N/A	N/A	ACTCCTCATTGACATCTACA	48	G	515
1475610	9090	9109	N/A	N/A	TATCAGCAGGTATCTATCTT	47	G	516
1475616	10469	10488	160	179	AAACTTCTCTGCTCCACCCC	23	G	517
1475619	12379	12398	804	823	ATGGGAGCATGATATCCAGT	32	G	518
1475633	10483	10502	174	193	GCAGCTGAATACAGAACTT	66	G	519
1475643	18655	18674	4140	4159	AAACAGCCACATCTAACAGA	66	G	520
1475646	18488	18507	3973	3992	CTGCACACCACATCGGGCCT	64	G	521
1475649	18143	18162	N/A	N/A	CGTACCATGCCACAGCTCC	74	G	522
1475652	15394	15413	3123	3142	AAGGGATCCAAGCCCGGCCC	100	G	523
1475653	6692	6711	N/A	N/A	TCATCTATAGCCCCTTCATC	75	G	524
1475656	4716	4735	N/A	N/A	GCCCCAATCGCCCGCCGCC	90	G	525
1475668	7047	7066	N/A	N/A	CCACTGCGCACTGCCATTAC	54	G	526
1475681	12163	12182	588	607	TGGTCGATATCCCTAGGGTC	16†	G	409
1475689	7373	7392	N/A	N/A	TTCACCTTCATTACCTTGCT	8	G	527
1475692	18663	18682	4148	4167	GCTACGCAAAACAGCCACAT	25	G	49
1475694	6584	6603	N/A	N/A	GTTCTATAGTATTTCCCCTG	6	G	528
1475701	12812	12831	1237	1256	AAGTCCACCCATACCCTGTC	37	G	25

1475705	9078	9097	N/A	N/A	TCTATCTTTATCCAAATCCC	64	G	529
1475708	9704	9723	N/A	N/A	ATACCTTCTTTATATCAAGC	10	G	530
1475710	17452	17471	3479	3498	TAAGGTGAGACCCCTGAGGCC	68	G	531
1475713	6504	6523	N/A	N/A	CCCAGCCATTTCTACAAGGT	77	G	532
1475722	15011	15030	N/A	N/A	CTGAGCCAACCTTCTGTGGGA	60	G	533
1475727	15097	15116	2826	2845	ACTGTAGCCACCGCACTGCC	84	G	534
1475732	15271	15290	3000	3019	GCAGCTGGATCACTGCTGTA	92	G	535
1475734	9161	9180	N/A	N/A	TTAAGCCTATCCTCCTACTT	78	G	536
1475735	12472	12491	897	916	GACAAAACCTCCACCAGTGCC	28	G	537
1475750	11055	11074	448	467	ACTCTCTGAGATCTCCTCAC	29	G	538
1475754	18675	18694	4160	4179	GTGGCACACGATGCTACGCA	73	G	539
1475755	10550	10569	N/A	N/A	CACCGAGTCTTTATTCTGTC	28	G	540
1475756	10849	10868	N/A	N/A	ACCTGAGGACAGAATACCTT	96	G	541
1475768	9640	9659	N/A	N/A	ATGGTAAGCATTATTACCCT	52	G	542
1475779	10166	10185	N/A	N/A	GAAGTATAATCTCTTTCATC	32	G	543
1475781	10425	10444	116	135	GAAGCAGGATCTCCAAGTTT	86	G	544
1475782	10377	10396	68	87	GATCTGTTTTCAATGAAACC	61	G	545
1475791	7355	7374	N/A	N/A	CTTTATTTTATTTATTTATT	77	G	546
1475795	18527	18546	4012	4031	TGTGCGCTTTCTGTCCCAT	27	G	547
1475810	9116	9135	N/A	N/A	TCACAGCCAATCCATCCGTA	24	G	548
1475817	14059	14078	2484	2503	CTGGGTACATCTACCACCTT	69	G	345
1475818	15353	15372	3082	3101	CAGCTCACTAGGCTTCACCT	46	G	549
1475819	18643	18662	4128	4147	CTAACAGATGAAATAATCAC	55	G	550
1475821	18285	18304	3770	3789	CGCTTTCCTTCTTCAGGTGA	45	G	551
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCT	9	H	483
1475360	18523	18542	4008	4027	CGCTTTCCTGTCCCATCCTC	34	H	552
1475363	4918	4937	N/A	N/A	GGCCGCAGACCTTACCTGCT	93	H	553
1475371	11818	11837	N/A	N/A	AAGCACCTTGTCTCTACCCA	65	H	554
1475380	8619	8638	N/A	N/A	TCTGAACCTTCAACTGATGC	62	H	555
1475382	12811	12830	1236	1255	AGTCCACCCATACCCTGTCC	32	H	556
1475385	10818	10837	362	381	TGGACTTCTCAGCTTTGCCA	25	H	557
1475391	12116	12135	541	560	CCCGTCCAAGCTATCCAGAT	13†	H	407
1475394	7352	7371	N/A	N/A	TATTTTATTTATTTATTTAT	86	H	558
1475402	18224	18243	N/A	N/A	AGACCAACTCTGACCTTGCC	83	H	559
1475407	1855	1874	N/A	N/A	GAGCTCTTCTCCCTTGTTTT	67	H	560
1475412	18670	18689	4155	4174	ACACGATGCTACGCAAAACA	34	H	561
1475425	9115	9134	N/A	N/A	CACAGCCAATCCATCCGTAT	33	H	562
1475441	7026	7045	N/A	N/A	TTACTTTAAAAAGAAAATGA	105	H	563
1475452	14271	14290	N/A	N/A	GCCTCAAAACCACCCCTGCA	87	H	564
1475461	12338	12357	763	782	TTCAAAGCTAGCCTCTGGCT	84	H	565
1475465	10233	10252	N/A	N/A	CCACAAGACATTGCTGGCAT	56	H	566
1475468	18639	18658	4124	4143	CAGATGAAATAATCACACCA	29	H	567
1475472	10462	10481	153	172	TCTGCTCCACCCCAAGTTCC	63	H	568
1475473	12471	12490	896	915	ACAAAACCTCCACCAGTGCCC	38	H	569
1475474	1066	1085	N/A	N/A	AGGACCAGACCTTCGCAGAA	91	H	206

1475485	10623	10642	N/A	N/A	GTTCTTCTTCTCTAGACCCT	48	H	570
1475487	10667	10686	N/A	N/A	CACTGTTCTTTACATTGCAC	93	H	571
1475502	15393	15412	3122	3141	AGGGATCCAAGCCCGGCCCA	92	H	572
1475509	11051	11070	444	463	TCTGAGATCTCCTCACTCCG	38	H	573
1475520	6581	6600	N/A	N/A	CTATAGTATTTCCCTGCAT	56	H	574
1475530	8744	8763	N/A	N/A	ACACAGTAATTCTCACTCAC	22	H	575
1475533	14519	14538	2661	2680	CGCTCCTTTTCTTCGCGCGC	88	H	576
1475539	15341	15360	3070	3089	CTTCACCTCAAAGCCAGGCT	75	H	577
1475544	13361	13380	1786	1805	GTGGGAGCTACCGCCCTCCA	81	H	578
1475548	7044	7063	N/A	N/A	CTGCGCACTGCCATTACCTT	35	H	579
1475551	6602	6621	N/A	N/A	ACAGGTCTCCTGGCTCCTGT	98	H	580
1475557	10164	10183	N/A	N/A	AGTATAATCTCTTTCATCTC	29	H	581
1475562	18487	18506	3972	3991	TGCACACCACATCGGGCCTT	63	H	582
1475582	7623	7642	N/A	N/A	GCCCTTCTTTTTTAATCACC	35	H	583
1475583	18284	18303	3769	3788	GCTTTCCTTCTTCAGGTGAC	32	H	584
1475586	10531	10550	222	241	CGTGTCTTCATTCTTCAGGC	57	H	585
1475587	12819	12838	1244	1263	CAGGAGGAAGTCCACCCATA	41	H	586
1475589	12584	12603	1009	1028	CCCAGAGCTTGATACTGAAA	37	H	587
1475592	11075	11094	468	487	GCATTGGTCTCCTCACTTTC	4†	H	588
1475593	18654	18673	4139	4158	AACAGCCACATCTAACAGAT	50	H	589
1475594	9088	9107	N/A	N/A	TCAGCAGGTATCTATCTTTA	6	H	590
1475598	18291	18310	3776	3795	GCTTGTGCGTTTCTTCTTTC	27	H	591
1475601	11037	11056	430	449	ACTCCGACCCTGCTTGTTGA	48	H	250
1475602	9077	9096	N/A	N/A	CTATCTTTATCCAAATCCCT	62	H	592
1475605	9155	9174	N/A	N/A	CTATCCTCCTACTTGGTGTA	45	H	387
1475623	11111	11130	N/A	N/A	CAAGGGTTTCCCACCTCAGT	87†	H	593
1475628	12220	12239	645	664	GAGTCATTCTCCACACTTCC	12	H	594
1475629	4689	4708	N/A	N/A	CAAACCCCGATCCCCGCTCT	64	H	595
1475634	16484	16503	N/A	N/A	GCTCATTATCGCCTATGACA	42	H	596
1475635	9703	9722	N/A	N/A	TACCTTCTTTATATCAAGCC	22	H	597
1475644	18662	18681	4147	4166	CTACGCAAAACAGCCACATC	55	H	438
1475648	10509	10528	200	219	TGGAGACCCCATCTCCTCT	91	H	598
1475660	18210	18229	N/A	N/A	CTTGCCCCCTCTTACCGAAG	95	H	599
1475662	14601	14620	N/A	N/A	CAGTGACGCACTCACCACGC	99	H	398
1475664	9639	9658	N/A	N/A	TGGTAAGCATTATTACCCTC	58	H	600
1475667	15351	15370	3080	3099	GCTCACTAGGCTTCACCTCA	23	H	601
1475670	18142	18161	N/A	N/A	GTACCATGCCACAGCTCCT	93	H	602
1475671	4696	4715	N/A	N/A	CCCGGAGCAAACCCCGATCC	86	H	603
1475676	8908	8927	N/A	N/A	GATTGACCTTTAAACCCACT	16	H	604
1475697	7379	7398	N/A	N/A	AGCACATTACCTTCATTAC	13	H	605
1475699	7372	7391	N/A	N/A	TCACCTTCATTACCTTGCTT	8	H	606
1475704	17557	17576	N/A	N/A	AACTTCCATCCTTACCAAAG	97	H	607
1475717	11392	11411	N/A	N/A	GACCACTTCTGCATTTTCCT	32	H	608
1475721	10422	10441	113	132	GCAGGATCTCCAAGTTTCCA	77	H	609
1475725	12145	12164	570	589	TCGCTGCTGCCATCATCATT	4†	H	610

1475737	10845	10864	N/A	N/A	GAGGACAGAATACCTTGGCT	83	H	611
1475749	10716	10735	260	279	TCCGTCCACTCCTCATTGAC	41	H	612
1475757	10759	10778	303	322	CCCCTCGATCTCAGTTCTTC	86	H	327
1475761	10480	10499	171	190	GCTGAATACAGAACTTCTC	32	H	613
1475774	14055	14074	2480	2499	GTACATCTACCACCTTGGGA	17	H	614
1475787	9068	9087	N/A	N/A	TCCAAATCCCTATAGCCAGC	7	H	615
1475789	12478	12497	903	922	GGTCCAGACAAAACCTCCACC	69	H	616
1475792	10561	10580	N/A	N/A	TCATTTTAACTCACCGAGTC	89	H	617
1475797	6502	6521	N/A	N/A	CAGCCATTTCTACAAGGTCA	57	H	618
1475804	15245	15264	2974	2993	CGGGACATTGTAACCCAGGA	67	H	430
1475809	12641	12660	1066	1085	TAGGTTCCCACCACCCACTG	57	H	619
1475811	15090	15109	2819	2838	CCACCGCACTGCCCGGTTCA	88	H	620
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTC	11	I	483
1475362	10758	10777	302	321	CCCTCGATCTCAGTTCTTCC	69	I	621
1475365	17556	17575	N/A	N/A	ACTTCCATCCTTACCAAAGA	88	I	622
1475366	14267	14286	N/A	N/A	CAAAACCACCCCTGCAGGCT	49	I	623
1475367	18494	18513	3979	3998	CCACCTCTGCACACCACATC	84	I	624
1475370	9483	9502	N/A	N/A	TTGCTGTATTCTCCTCAGAA	40	I	625
1475372	11375	11394	N/A	N/A	CCTTAAGATTTATTTGTTCC	45	I	626
1475377	9066	9085	N/A	N/A	CAAATCCCTATAGCCAGCTG	34	I	627
1475381	12817	12836	1242	1261	GGAGGAAGTCCACCCATACC	56	I	103
1475383	12810	12829	1235	1254	GTCCACCCATACCCTGTCCC	32	I	628
1475386	10477	10496	168	187	GAATACAGAACTTCTCTGC	48	I	629
1475387	4915	4934	N/A	N/A	CGCAGACCTTACCTGCTGGT	82	I	630
1475388	10530	10549	221	240	GTGTCTTCATTCTTCAGGCT	83	I	631
1475403	12542	12561	967	986	CTGCTTACCCCCATTAGGGC	58	I	257
1475411	14481	14500	2623	2642	CCGCACCTTCTCCACCAGGT	68	I	632
1475426	15557	15576	3286	3305	CCTCTCAGCTGCCAGCCGCT	71	I	633
1475440	10163	10182	N/A	N/A	GTATAATCTCTTTCATCTCT	22	I	634
1475442	18667	18686	4152	4171	CGATGCTACGAAAACAGCC	46	I	127
1475459	11049	11068	442	461	TGAGATCTCCTCACTCCGAC	25	I	406
1475462	8735	8754	N/A	N/A	TTCTCACTCACCTCCACGGA	56	I	635
1475470	10560	10579	N/A	N/A	CATTTTAACTCACCGAGTCT	90	I	636
1475476	18290	18309	3775	3794	CTTGTCGCTTTCCTTCTTCA	30	I	637
1475483	15340	15359	3069	3088	TTCACCTCAAAGCCAGGCTT	81	I	638
1475494	12637	12656	1062	1081	TTCCCAACCACCACTGGAGT	90	I	639
1475495	13992	14011	2417	2436	TCTCATACTCCTCAGCCGGC	76	I	640
1475499	18475	18494	3960	3979	CGGGCCTTGGCCTTCTGTCT	89	I	641
1475501	15380	15399	3109	3128	CGGCCCAGGGACCCCATGTA	82	I	642
1475507	9087	9106	N/A	N/A	CAGCAGGTATCTATCTTTAT	3	I	643
1475516	18652	18671	4137	4156	CAGCCACATCTAACAGATGA	66	I	644
1475517	12217	12236	642	661	TCATTCTCCACACTTCCAGG	11	I	645
1475521	10652	10671	N/A	N/A	TGCACCTAACTTTATGGTGC	93	I	646
1475524	6288	6307	N/A	N/A	CGTTTTCATCTCCCATCAT	66	I	647
1475538	18151	18170	N/A	N/A	TGCCCAGCCGTACCATGCCC	80	I	648

1475554	1064	1083	N/A	N/A	GACCAGACCTTCGCAGAAGC	84	I	649
1475555	10618	10637	N/A	N/A	TCTTCTCTAGACCCTTCCTC	84	I	650
1475558	15042	15061	2771	2790	GAGATGGGCATTCCACCGGA	64	I	271
1475561	7485	7504	N/A	N/A	TGTCTTTCTAGACCTGGGTC	35	I	651
1475568	7023	7042	N/A	N/A	CTTTAAAAAGAAAATGATTA	88	I	652
1475573	1748	1767	N/A	N/A	AACCATTGTCTACCCTCTCC	82	I	653
1475584	7378	7397	N/A	N/A	GCACATTCACCTTCATTACC	9	I	654
1475595	18223	18242	N/A	N/A	GACCAACTCTGACCTTGCCC	90	I	655
1475604	4633	4652	N/A	N/A	CCGCCCCGAATGCCCCGGGC	89	I	656
1475606	10418	10437	109	128	GATCTCCAAGTTTCCAGTGT	49	I	657
1475609	14598	14617	N/A	N/A	TGACGCACTCACCACGCTGC	77	I	658
1475611	12477	12496	902	921	GTCCAGACAAAACCTCCACCA	25	I	659
1475615	7041	7060	N/A	N/A	CGCACTGCCATTACCTTACT	32	I	660
1475622	11110	11129	N/A	N/A	AAGGGTTTCCCACCTCAGTT	86†	I	661
1475625	12470	12489	895	914	CAAAACTCCACCAGTGCCCC	66	I	662
1475632	9114	9133	N/A	N/A	ACAGCCAATCCATCCGTATC	38	I	231
1475638	10461	10480	152	171	CTGCTCCACCCCAAGTTCCC	62	I	663
1475650	10715	10734	259	278	CCGTCCACTCCTCATTGACA	32	I	664
1475651	8907	8926	N/A	N/A	ATTGACCTTTAAACCCACTA	16	I	665
1475661	9702	9721	N/A	N/A	ACCTTCTTTATATCAAGCCC	7	I	666
1475669	7342	7361	N/A	N/A	ATTTATTTATTTATTTATTT	89	I	667
	7346	7365						
1475673	8612	8631	N/A	N/A	TTTCAACTGATGCTCTGCCC	93	I	668
1475678	10170	10189	N/A	N/A	GCTCGAAGTATAATCTCTTT	21	I	669
1475685	11073	11092	466	485	ATTGGTCTCCTCACTTTCAC	5†	I	670
1475690	6599	6618	N/A	N/A	GGTCTCCTGGCTCCTGTTCT	64	I	671
1475707	18115	18134	N/A	N/A	TCGCTGAGCCCATGTCCCCT	93	I	672
1475711	4695	4714	N/A	N/A	CCGGAGCAAACCCCGATCCC	73	I	59
1475718	12115	12134	540	559	CCGTCCAAGCTATCCAGATC	16†	I	329
1475720	6578	6597	N/A	N/A	TAGTATTTCCCCTGCATGAA	24	I	673
1475730	12240	12259	665	684	ACAGGCCAGAAGATGAGTCA	60	I	674
1475731	13105	13124	1530	1549	TGGCTCCACACAGCCTGGGA	79	I	675
1475747	10507	10526	198	217	GAGACCCCATCTCCTCTGC	38	I	676
1475751	7370	7389	N/A	N/A	ACCTTCATTACCTTGCTTTA	16	I	677
1475752	18661	18680	4146	4165	TACGCAAAACAGCCACATCT	60	I	678
1475760	15349	15368	3078	3097	TCACTAGGCTTCACCTCAAA	38	I	679
1475770	9128	9147	N/A	N/A	TTACACAGTTTCTCACAGCC	13	I	680
1475775	11036	11055	429	448	CTCCGACCCTGCTTGTTGAC	45	I	681
1475778	18233	18252	N/A	N/A	AGAGACTTGAGACCAACTCT	91	I	682
1475783	10810	10829	354	373	TCAGCTTTGCCATCACTGCT	24	I	683
1475784	11816	11835	N/A	N/A	GCACCTTGTCTCTACCCACA	54	I	684
1475785	18637	18656	4122	4141	GATGAAATAATCACACCAAC	26	I	685
1475794	10841	10860	N/A	N/A	ACAGAATACCTTGGCTGTCT	98	I	686
1475800	12139	12158	564	583	CTGCCATCATCATTAAGGCT	54†	I	687
1475802	9076	9095	N/A	N/A	TATCTTTATCCAAATCCCTA	81	I	688

1475815	15241	15260	2970	2989	ACATTGTAACCCAGGAGCCC	93	I	352
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCC	10	J	483
1475361	10506	10525	197	216	AGACCCCATTTCTCCTCTGCC	29	J	689
1475375	9126	9145	N/A	N/A	ACACAGTTTCTCACAGCCAA	5	J	690
1475389	18660	18679	4145	4164	ACGCAAAACAGCCACATCTA	37	J	691
1475392	18072	18091	3749	3768	TGTAGTAGTCCTCCTGGGCA	70	J	692
1475396	15550	15569	3279	3298	GCTGCCAGCCGCTCAGCATA	78	J	693
1475398	9085	9104	N/A	N/A	GCAGGTATCTATCTTTATCC	4	J	694
1475404	6575	6594	N/A	N/A	TATTTCCCCTGCATGAAGCT	42	J	695
1475408	6212	6231	N/A	N/A	GTTCCAACAGACTTCAACAT	81	J	696
1475409	10097	10116	N/A	N/A	GATCACACAGTTTACCCTTC	14	J	697
1475414	14081	14100	2506	2525	CCTGGCAGACTGACTGGCAT	41	J	698
1475429	7367	7386	N/A	N/A	TTCATTACCTTGCTTTATTT	39	J	699
1475432	4914	4933	N/A	N/A	GCAGACCTTACCTGCTGGTA	116	J	700
1475435	12138	12157	563	582	TGCCATCATCATTAAAGGCTC	98†	J	701
1475450	18289	18308	3774	3793	TTGTCGCTTTTCTTCTCAG	27	J	702
1475453	17554	17573	N/A	N/A	TTCCATCCTTACCAAAGAGC	81	J	703
1475456	9105	9124	N/A	N/A	CCATCCGTATCTGTCTATCA	17	J	704
1475463	12112	12131	537	556	TCCAAGCTATCCAGATCGGA	28†	J	705
1475464	10460	10479	151	170	TGCTCCACCCCAAGTTCCCC	71	J	706
1475467	1021	1040	N/A	N/A	AGCCTTGAAGTTCTCCAC	83	J	707
1475478	7929	7948	N/A	N/A	TCAACTACAGCTATTTTCCC	44	J	708
1475488	10807	10826	351	370	GCTTTGCCATCACTGCTGGA	17	J	709
1475490	10558	10577	N/A	N/A	TTTAACTCACCGAGTCTTT	99	J	710
1475491	12937	12956	1362	1381	GCTGCAGAGCTACTACTAGA	20	J	711
1475493	1746	1765	N/A	N/A	CCATTGTCTACCCTCTCCCA	96	J	712
1475498	10714	10733	258	277	CGTCCACTCCTCATTGACAT	44	J	713
1475500	12816	12835	1241	1260	GAGGAAGTCCACCCATACCC	36	J	714
1475508	12808	12827	1233	1252	CCACCCATACCCTGTCCCAT	38	J	715
1475514	7377	7396	N/A	N/A	CACATTACCTTCATTACCT	32	J	716
1475535	12476	12495	901	920	TCCAGACAAAACCTCCACCAG	49	J	717
1475537	10395	10414	86	105	CACCTGGAACCTTTTGCAGGA	90	J	718
1475552	18650	18669	4135	4154	GCCACATCTAACAGATGAAA	55	J	719
1475553	18222	18241	N/A	N/A	ACCAACTCTGACCTTGCCCC	78	J	720
1475574	10169	10188	N/A	N/A	CTCGAAGTATAATCTCTTTC	10	J	721
1475576	10824	10843	368	387	TCTGCCTGGACTTCTCAGCT	64	J	722
1475577	11034	11053	427	446	CCGACCCTGCTTGTTGACCT	41	J	172
1475578	18636	18655	4121	4140	ATGAAATAATCACACCAACG	28	J	723
1475580	12541	12560	966	985	TGCTTACCCCCATTAGGGCC	64	J	179
1475581	4694	4713	N/A	N/A	CGGAGCAAACCCCGATCCCC	62	J	724
1475590	13991	14010	2416	2435	CTCATACTCCTCAGCCGGCT	61	J	725
1475612	11109	11128	N/A	N/A	AGGGTTTCCACCTCAGTTT	54†	J	726
1475613	12595	12614	1020	1039	GCACCACTAGCCCCAGAGCT	48	J	727
1475621	9277	9296	N/A	N/A	AAGGACCCATTCTCTAGTAC	47	J	728
1475631	9701	9720	N/A	N/A	CCTTCTTTATATCAAGCCCT	13	J	729

1475636	15299	15318	3028	3047	TTCACGGGCTTCCCGTTCCC	73	J	730
1475641	8689	8708	N/A	N/A	TGAGTCTAACCTTTCCAGGA	24	J	731
1475658	11047	11066	440	459	AGATCTCCTCACTCCGACCC	8	J	732
1475659	15347	15366	3076	3095	ACTAGGCTTCACCTCAAAGC	61	J	733
1475663	4522	4541	N/A	N/A	GCAGCCCGCACCCGCGCGAT	34	J	734
1475666	9075	9094	N/A	N/A	ATCTTTATCCAAATCCCTAT	60	J	735
1475674	18418	18437	3903	3922	CCCTGCAACTGAGCAGCACC	93	J	736
1475675	18230	18249	N/A	N/A	GACTTGAGACCAACTCTGAC	82	J	737
1475683	12225	12244	650	669	AGTCAGAGTCATTCTCCACA	5	J	738
1475693	8906	8925	N/A	N/A	TTGACCTTTAAACCCACTAA	39	J	739
1475695	11062	11081	455	474	CACTTTCCTCTCTGAGATC	26	J	740
1475706	12215	12234	640	659	ATTCTCCACACTTCCAGGGC	38	J	741
1475716	10639	10658	N/A	N/A	ATGGTGCACATTATTTGTTC	94	J	742
1475724	10513	10532	204	223	GCTGTGGAGACCCCATTCCTC	50	J	743
1475733	6596	6615	N/A	N/A	CTCCTGGCTCCTGTTCTATA	37	J	744
1475740	10475	10494	166	185	ATACAGAACTTCTCTGCTC	66	J	745
1475742	10757	10776	301	320	CCTCGATCTCAGTTCTTCCC	53	J	746
1475743	7037	7056	N/A	N/A	CTGCCATTACCTTACTTTAA	29	J	747
1475744	7459	7478	N/A	N/A	TAGCACCAGCCTACACTCCT	36	J	748
1475748	18491	18510	3976	3995	CCTCTGCACACCACATCGGG	71	J	749
1475762	11759	11778	N/A	N/A	CACCACTTTAACCATCCTCC	77	J	750
1475764	15359	15378	3088	3107	GGGTTCCAGCTCACTAGGCT	62	J	751
1475765	12464	12483	889	908	TCCACCAGTGCCCCCAGGAT	60	J	752
1475773	7341	7360	N/A	N/A	TTTATTTATTTATTTATTTA	93	J	753
	7345	7364						
	7349	7368						
1475776	18666	18685	4151	4170	GATGCTACGCAAAACAGCCA	43	J	754
1475780	6700	6719	N/A	N/A	AGATCATCTCATCTATAGCC	27	J	755
1475786	14480	14499	2622	2641	CGCACCTTCTCCACCAGGTC	96	J	756
1475798	9053	9072	N/A	N/A	CCAGCTGTATTCATTGTCAC	31	J	757
1475806	14597	14616	N/A	N/A	GACGCACTCACCACGCTGCG	91	J	758
1475807	18148	18167	N/A	N/A	CCAGCCGTACCATGCCCAACA	70	J	759
1475808	10615	10634	N/A	N/A	TCTCTAGACCCTTCCTCCTA	57	J	760
1475812	15040	15059	2769	2788	GATGGGCATTCCACCGGAGC	49	J	193
1475814	15174	15193	2903	2922	CAGGAGACATGACATGAGGC	24	J	761
1475820	11236	11255	N/A	N/A	CAGAACTGCTCTCATAAGCA	77	J	762
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCC	13	K	483
1475405	14442	14461	2584	2603	CTTGAGCCCTCCAGTGGCA	63	K	763
1475406	18659	18678	4144	4163	CGCAAAACAGCCACATCTAA	50	K	764
1475415	9084	9103	N/A	N/A	CAGGTATCTATCTTTATCCA	16	K	765
1475416	10823	10842	367	386	CTGCCTGGACTTCTCAGCTT	72	K	766
1475417	9276	9295	N/A	N/A	AGGACCCATTCTCTAGTACT	93	K	767
1475418	13990	14009	2415	2434	TCATACTCCTCAGCCGGCTC	72	K	768
1475420	7376	7395	N/A	N/A	ACATTCACCTTCATTACCTT	20	K	769
1475422	7364	7383	N/A	N/A	ATTACCTTGCTTTATTTTAT	14	K	770

1475423	11006	11025	399	418	GAGGCTTCCTCTACTCGGGC	13	K	771
1475424	6593	6612	N/A	N/A	CTGGCTCCTGTTCTATAGTA	68	K	772
1475428	10474	10493	165	184	TACAGAAACTTCTCTGCTCC	65	K	773
1475431	15346	15365	3075	3094	CTAGGCTTCACCTCAAAGCC	90	K	774
1475433	12934	12953	1359	1378	GCAGAGCTACTACTAGAGGA	4	K	337
1475434	12223	12242	648	667	TCAGAGTCATTCTCCACACT	27	K	775
1475436	10566	10585	N/A	N/A	GTCTCTCATTTTAACTCACC	85	K	776
1475439	10725	10744	269	288	CCTCTTTCTTCCGTCCACTC	34	K	777
1475443	15297	15316	3026	3045	CACGGGCTTCCCGTCCCTC	80	K	778
1475449	12214	12233	639	658	TTCTCCACACTTCCAGGGCT	39	K	779
1475454	7035	7054	N/A	N/A	GCCATTACCTTACTTTAAAA	30	K	780
1475455	9072	9091	N/A	N/A	TTTATCCAAATCCCTATAGC	62	K	781
1475458	6572	6591	N/A	N/A	TTCCCCCTGCATGAAGCTGTT	62	K	782
1475469	10393	10412	84	103	CCTGGAACCTTTTGAGGATC	98	K	783
1475475	14523	14542	2665	2684	CTCGCGCTCCTTTTCTTCGC	37	K	784
1475481	15155	15174	2884	2903	CCGGGCATATTCACTGAGAG	58	K	785
1475492	11728	11747	N/A	N/A	CCTTGTTTTTATACCACTT	81	K	786
1475505	9052	9071	N/A	N/A	CAGCTGTATTCAATTGCACT	37	K	787
1475506	18649	18668	4134	4153	CCACATCTAACAGATGAAAT	64	K	788
1475512	4745	4764	N/A	N/A	CGGCCCCCATCCCCCTTTT	76	K	789
1475518	15358	15377	3087	3106	GGTTCAGCTCACTAGGCTT	68	K	354
1475523	18542	18561	4027	4046	CCTGGTCCAAGATTCTGTGC	40	K	790
1475529	12463	12482	888	907	CCACCAGTGCCCCCAGGATA	46	K	791
1475532	11044	11063	437	456	TCTCCTCACTCCGACCTGC	15	K	792
1475534	17560	17579	N/A	N/A	CCCAACTTCCATCCTTACCA	87	K	793
1475543	8880	8899	N/A	N/A	TAGGTCTTTCTTCCTGAATT	43	K	794
1475545	12540	12559	965	984	GCTTACCCCCATTAGGGCCC	65	K	101
1475549	11997	12016	N/A	N/A	GCATAAAATCATTCCCCTC	64	K	795
1475559	10553	10572	N/A	N/A	ACTCACCGAGTCTTTATTCT	105	K	796
1475579	17553	17572	N/A	N/A	TCCATCCTTACCAAAGAGCT	89	K	797
1475591	1020	1039	N/A	N/A	GCCTTGAAGTTCTCCCACT	99	K	798
1475597	7390	7409	N/A	N/A	GCCACATACTAAGCACATTC	19	K	799
1475600	18287	18306	3772	3791	GTCGCTTTCCTTCTTCAGGT	30	K	800
1475603	11102	11121	N/A	N/A	CCCACCTCAGTTTTGGTCTT	73†	K	801
1475617	12815	12834	1240	1259	AGGAAGTCCACCCATACCCT	61	K	802
1475624	7053	7072	N/A	N/A	CGTGAGCCACTGCGCACTGC	104	K	803
1475630	4692	4711	N/A	N/A	GAGCAAACCCCGATCCCCGC	26	K	804
1475639	14062	14081	2487	2506	TGGCTGGGTACATCTACCAC	27	K	34
1475640	15546	15565	3275	3294	CCAGCCGCTCAGCATAGGAC	81	K	805
1475654	10454	10473	145	164	ACCCCAAGTTCCCCACAGCT	36	K	806
1475655	10711	10730	N/A	N/A	CCACTCCTCATTGACATCTA	25	K	807
1475657	1074	1093	N/A	N/A	AGGGAGCCAGGACCAGACCT	71	K	808
1475682	10168	10187	N/A	N/A	TCGAAGTATAATCTCTTTCA	17	K	809
1475684	2734	2753	N/A	N/A	GCTCAATCCCACTTGTCTA	100	K	810
1475686	15039	15058	2768	2787	ATGGGCATTCCACCGGAGCA	42	K	811

1475687	9096	9115	N/A	N/A	TCTGTCTATCAGCAGGTATC	39	K	812
1475698	11223	11242	N/A	N/A	ATAAGCACTATGATCTGGCC	97	K	813
1475700	18145	18164	N/A	N/A	GCCGTACCATGCCCACAGCT	94	K	814
1475702	12805	12824	1230	1249	CCCATACCCTGTCCCATGGC	75	K	815
1475703	12475	12494	900	919	CCAGACAAAACCTCCACCAGT	40	K	816
1475709	18409	18428	3894	3913	TGAGCAGCACCTCTTGGCT	77	K	817
1475712	10638	10657	N/A	N/A	TGGTGCACATTATTTGTTCT	72	K	818
1475715	5743	5762	N/A	N/A	TGCTCAATTCTCCATTCCA	15	K	819
1475719	8632	8651	N/A	N/A	ACAGAGCCTATCTTCTGAAC	82	K	820
1475723	18220	18239	N/A	N/A	CAACTCTGACCTTGCCCCCT	90	K	821
1475726	10763	10782	307	326	CCGGCCCCCTCGATCTCAGTT	75	K	405
1475728	6698	6717	N/A	N/A	ATCATCTCATCTATAGCCCC	26	K	822
1475741	10095	10114	N/A	N/A	TCACACAGTTTACCCTTCAT	20	K	823
1475753	18490	18509	3975	3994	CTCTGCACACCACATCGGGC	55	K	824
1475758	12137	12156	562	581	GCCATCATCATTAAGGCTCC	30†	K	825
1475759	10512	10531	203	222	CTGTGGAGACCCCATCTCC	72	K	826
1475763	11060	11079	453	472	CTTTCACCTCTGAGATCTC	14	K	827
1475767	18665	18684	4150	4169	ATGCTACGCAAAACAGCCAC	46	K	828
1475788	18229	18248	N/A	N/A	ACTTGAGACCAACTCTGACC	100	K	829
1475790	12594	12613	1019	1038	CACCACTAGCCCCAGAGCTT	85	K	830
1475793	7923	7942	N/A	N/A	ACAGCTATTTTCCCACATTT	20	K	831
1475796	10487	10506	178	197	CTGGGCAGCTGAATACAGAA	32	K	832
1475803	9700	9719	N/A	N/A	CTTCTTTATATCAAGCCCTT	32	K	833
1475816	9120	9139	N/A	N/A	TTTCTCACAGCCAATCCATC	59	K	834
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCC	8	L	483
1475364	7050	7069	N/A	N/A	GAGCCACTGCGCACTGCCAT	75	L	835
1475368	10724	10743	268	287	CTCTTTCTTCCGTCCACTCC	51	L	836
1475369	10551	10570	N/A	N/A	TCACCGAGTCTTTATTCTGT	41	L	837
1475373	11726	11745	N/A	N/A	TTGGTTTTTATACCACTTCT	69	L	838
1475376	15154	15173	2883	2902	CGGGCATATTTACTGAGAGT	20	L	839
1475378	17559	17578	N/A	N/A	CCAACCTCCATCCTTACCAA	93	L	840
1475384	7374	7393	N/A	N/A	ATTCACCTTCATTACCTTGC	5	L	841
1475390	10710	10729	N/A	N/A	CACTCCTCATTGACATCTAC	66	L	842
1475393	10053	10072	N/A	N/A	ACACACACATTCCACGGAGC	17	L	843
1475399	8911	8930	N/A	N/A	TGTGATTGACCTTTAAACCC	19	L	844
1475401	14285	14304	N/A	N/A	TGCTTGTAGCCCCCGCCTCA	56	L	845
1475410	8626	8645	N/A	N/A	CCTATCTTCTGAACTTTCAA	45	L	846
1475421	14521	14540	2663	2682	CGCGCTCCTTTTCTTCGCGC	80	L	847
1475427	17552	17571	N/A	N/A	CCATCCTTACCAAAGAGCTG	87	L	848
1475430	1069	1088	N/A	N/A	GCCAGGACCAGACCTTCGCA	100	L	284
1475445	13981	14000	2406	2425	TCAGCCGGCTCCTGTTTGAT	71	L	849
1475451	6590	6609	N/A	N/A	GCTCCTGTTCTATAGTATTT	58	L	850
1475460	12539	12558	964	983	CTTACCCCCATTAGGGCCCC	82	L	851
1475480	10379	10398	70	89	AGGATCTGTTTTCAATGAAA	34	L	852
1475482	15357	15376	3086	3105	GTTCCAGCTCACTAGGCTTC	48	L	853

1475489	15545	15564	3274	3293	CAGCCGCTCAGCATAGGACA	68	L	854
1475503	12133	12152	558	577	TCATCATTAAGGCTCCGCCC	15†	L	855
1475515	4691	4710	N/A	N/A	AGCAAACCCCGATCCCCGCT	37	L	856
1475519	7718	7737	N/A	N/A	ATCACAGAACCTGTTACCA	32	L	857
1475526	12473	12492	898	917	AGACAAAACCTCCACCAGTGC	19	L	858
1475528	10565	10584	N/A	N/A	TCTCTCATTTTAACTCACCG	98	L	859
1475531	8839	8858	N/A	N/A	GAACAGACTAAGCTTACCCA	26	L	860
1475536	9119	9138	N/A	N/A	TTCTCACAGCCAATCCATCC	39	L	861
1475540	15015	15034	N/A	N/A	CCTCCTGAGCCAACTTCTGT	67	L	862
1475546	10167	10186	N/A	N/A	CGAAGTATAATCTCTTTCAT	43	L	863
1475556	9686	9705	N/A	N/A	GCCCTTCACATACATGATTT	51	L	864
1475560	18318	18337	3803	3822	GCTCTCTTGATCGCAGGTTT	30	L	865
1475566	10452	10471	143	162	CCCAAGTTCCCCACAGCTGT	67	L	866
1475569	9093	9112	N/A	N/A	GTCTATCAGCAGGTATCTAT	12	L	867
1475570	18228	18247	N/A	N/A	CTTGAGACCAACTCTGACCT	82	L	868
1475571	12813	12832	1238	1257	GAAGTCCACCCATACCCTGT	72	L	869
1475572	5742	5761	N/A	N/A	GCTCAATTCTCCATTTCAT	5	L	870
1475575	11004	11023	397	416	GGCTTCCTCTACTCGGGCCT	83	L	871
1475585	7032	7051	N/A	N/A	ATTACCTTACTTTAAAAAGA	87	L	872
1475588	6562	6581	N/A	N/A	TGAAGCTGTTTCACAGCCCT	84	L	873
1475596	11949	11968	N/A	N/A	GAGTACTCTTGCTCAAGCCC	111	L	85
1475599	18664	18683	4149	4168	TGCTACGCAAAACAGCCACA	36	L	874
1475607	1015	1034	N/A	N/A	GAAGTTCCTCCCACTTGCG	112	L	875
1475608	7387	7406	N/A	N/A	ACATACTAAGCACATTACC	27	L	876
1475614	12164	12183	589	608	CTGGTCGATATCCCTAGGGT	14†	L	20
1475618	18219	18238	N/A	N/A	AACTCTGACCTTGCCCCCTC	95	L	877
1475620	11043	11062	436	455	CTCCTCACTCCGACCCTGCT	19	L	878
1475626	11115	11134	N/A	N/A	GCGACAAGGGTTTCCCACCT	81†	L	879
1475627	6694	6713	N/A	N/A	TCTCATCTATAGCCCCTTCA	26	L	880
1475637	10471	10490	162	181	AGAAACTTCTCTGCTCCACC	28	L	881
1475642	18645	18664	4130	4149	ATCTAACAGATGAAATAATC	64	L	882
1475645	12645	12664	1070	1089	AAGGTAGGTTCCCACCACCC	72	L	883
1475647	7358	7377	N/A	N/A	TTGCTTTATTTTATTTATT	92	L	884
1475665	12411	12430	836	855	GAGCCTGGAACATTCGAGAT	11	L	885
1475672	10822	10841	366	385	TGCCTGGACTTCTCAGCTTT	78	L	886
1475677	18286	18305	3771	3790	TCGCTTTCCTTCTTCAGGTG	43	L	887
1475679	18489	18508	3974	3993	TCTGCACACCACATCGGGCC	62	L	888
1475680	15296	15315	3025	3044	ACGGGCTTCCCGTTCCCTCT	77	L	353
1475688	10762	10781	306	325	CGGCCCCCTCGATCTCAGTTC	75	L	889
1475691	10486	10505	177	196	TGGGCAGCTGAATACAGAAA	30	L	890
1475696	2117	2136	N/A	N/A	TGGCACTCACTTTACCACTC	106	L	891
1475714	15345	15364	3074	3093	TAGGCTTCACCTCAAAGCCA	90	L	892
1475729	12592	12611	1017	1036	CCACTAGCCCCAGAGCTTGA	64	L	893
1475736	14060	14079	2485	2504	GCTGGGTACATCTACCACCT	59	L	423
1475738	18144	18163	N/A	N/A	CCGTACCATGCCACAGCTC	80	L	894

1475739	18658	18677	4143	4162	GCAAAACAGCCACATCTAAC	30	L	895
1475745	9079	9098	N/A	N/A	ATCTATCTTTATCCAAATCC	60	L	896
1475746	10625	10644	N/A	N/A	TTGTTCTTCTTCTCTAGACC	65	L	897
1475766	4737	4756	N/A	N/A	ATCCCCCCTTTCCCGCCT	40	L	898
1475769	18529	18548	4014	4033	TCTGTGCGCTTTCTGTCCCC	19	L	899
1475771	9166	9185	N/A	N/A	AGTTTTTAAGCCTATCCTCC	52	L	900
1475772	11093	11112	486	505	GTTTTGGTCTTTTTTGGTGC	2†	L	901
1475777	11059	11078	452	471	TTTCACTCTCTGAGATCTCC	22	L	902
1475799	12222	12241	647	666	CAGAGTCATTCTCCACACTT	20	L	903
1475801	12933	12952	1358	1377	CAGAGCTACTACTAGAGGAT	8	L	259
1475805	10511	10530	202	221	TGTGGAGACCCATTCTCCT	113	L	904
1475813	9070	9089	N/A	N/A	TATCCAAATCCCTATAGCCA	39	L	905

Example 5: Effect of 5-10-5 MOE gapmers complementary to human ATN1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to a human ATN RNA were designed and tested for their single dose effects on ATN1 RNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had the same culture conditions.

The modified oligonucleotides in the table below are 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeee; wherein "e" represents a 2'-MOE ribosyl sugar moiety, and each "d" represents a 2'-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the table below is 100% complementary to SEQ ID NO: 1 (GenBank Accession No. NC_000012.12 truncated from nucleosides 6923463 to 6943321), to SEQ ID NO: 2 (GenBank Accession No. NM_001940.3), or to both. 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular target nucleic acid sequence.

Cultured A431 cells were treated with modified oligonucleotide at a concentration of 1,000 nM by free uptake at a density of 7,000 cells per well. After a treatment period of 48 hours, total RNA was isolated from the cells and ATN1 RNA levels were measured by quantitative real-time RT-PCR. ATN1 RNA levels were measured by human primer-probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA relative to the amount of ATN1 RNA in untreated control cells (% UTC). The values marked with a "†" indicate that the modified oligonucleotide is complementary to the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of the modified oligonucleotides complementary to the amplicon region. Each separate experiment described in this example is identified by an Assay Identification letter in the table column labeled "AID".

Table 8

Reduction of ATN1 RNA by 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages in A-431 cells

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATN1 RNA (% UTC)	AID	SEQ ID NO
1441020	12041	12060	N/A	N/A	TTTCTCTTTTCCTTTCTCTGC	107	M	906
1572362	8788	8807	N/A	N/A	GTAAACGGCATGTCCATATT	46	M	907
1572376	6824	6843	N/A	N/A	TGGACCTGCCAGACTAACAA	77	M	908
1572379	5357	5376	N/A	N/A	TGTTCTGGTCCTTTGGAGCT	115	M	909
1572380	12083	12102	508	527	TGGCCGAGGGAGTTCTTGCT	15†	M	910
1572403	7875	7894	N/A	N/A	ATACTATCAACCAAAAAAAAA	110	M	911
1572414	5066	5085	N/A	N/A	CCAGGCAGAGCCCCGAGTGG	98	M	912
1572432	14526	14545	2668	2687	GCGCTCGCGCTCCTTTTCTT	84	M	913
1572466	7662	7681	N/A	N/A	ACACAGGAATGTACCTGAGG	78	M	914
1572482	6402	6421	N/A	N/A	TAGAAAATGAAAGAAAGTGC	109	M	915
1572532	6380	6399	N/A	N/A	AGAAGCAAAAAGACAACCTCT	109	M	916
1572542	14091	14110	N/A	N/A	TGGCCGCTCACCTGGCAGAC	93	M	917
1572558	6456	6475	N/A	N/A	GGAAAGAGGAAAAGGGTTAC	102	M	918
1572571	6583	6602	N/A	N/A	TTCTATAGTATTTCCCTGC	63	M	919
1572598	11982	12001	N/A	N/A	CCCTCACAGCACACTGTTGT	113	M	920
1572601	12203	12222	628	647	TCCAGGGCTGTAGATACTGG	102	M	921
1572670	11936	11955	N/A	N/A	CAAGCCCACCTCTTACCATC	90	M	922
1572682	11768	11787	N/A	N/A	TCTCATAACCACCACTTTAA	93	M	923
1572683	13665	13684	2090	2109	CTGCTGGCGAGGAAGCCACG	93	M	924
1572689	5291	5310	N/A	N/A	CATTCTGCCTTCGCCCCGAA	102	M	925
1572714	7617	7636	N/A	N/A	CTTTTTTAATCACCTGAAAT	114	M	926
1572717	11042	11061	435	454	TCCTCACTCCGACCCTGCTT	34	M	927
1572730	7746	7765	N/A	N/A	TAGAGAAGGGTGTCCATCTC	73	M	928
1572736	9502	9521	N/A	N/A	ATGCTCTTTCTTCTATACTT	53	M	929
1572823	7033	7052	N/A	N/A	CATTACCTTACTTTAAAAAG	103	M	930
1572828	13432	13451	1857	1876	AGGTGTGCTGGCCCTGGTGG	38	M	931
1572843	7642	7661	N/A	N/A	AACACAGCAATCATAGTATG	95	M	932
1572850	16460	16479	N/A	N/A	AACCCAAAGCTACAGGGCCC	100	M	933
1572886	18777	18796	4262	4281	CGTCATATAGATATTTATAT	53	M	934
1572906	11893	11912	N/A	N/A	ATTCTTGGCTGCTCCCTAGC	95	M	935
1572917	6318	6337	N/A	N/A	TGCCAAAAGATGGTGTAAACC	63	M	936
1572918	17631	17650	N/A	N/A	CCAAGCCCAACTAGGCCCAT	99	M	937
1572928	6693	6712	N/A	N/A	CTCATCTATAGCCCCCTCAT	76	M	938
1572942	12332	12351	757	776	GCTAGCCTCTGGCTGTCGAG	70	M	939
1572957	6424	6443	N/A	N/A	GCTCAAAGAGGAATTCAAGT	103	M	940
1572980	7768	7787	N/A	N/A	GGTGTATTTTGGCAGCCCT	61	M	941
1572991	7553	7572	N/A	N/A	CATAAAAGAACAAGTAATCC	109	M	942
1573036	6729	6748	N/A	N/A	AGAATCCGGGACCTTCAGAG	68	M	943
1573053	9011	9030	N/A	N/A	GTCAAGTCCCTCCAAATTAC	30	M	944

1573059	13629	13648	2054	2073	AAAGGGTAGCCGAAGAGGTG	65	M	945
1573066	7006	7025	N/A	N/A	TTAAGACCAGACTGGGTGG	92	M	946
1573096	13834	13853	2259	2278	CCTGGGCCTGCAGGTGGCGA	97	M	947
1573130	7484	7503	N/A	N/A	GTCTTTCTAGACCTGGGTCA	50	M	948
1573152	11796	11815	N/A	N/A	GCTGACTCCAACCTCCCTGTC	98	M	949
1573173	18524	18543	4009	4028	GCGCTTTCTGTCCCCATCCT	61	M	950
1573176	7416	7435	N/A	N/A	ATTACAGAGCACCTACTCTG	95	M	951
1573214	6761	6780	N/A	N/A	GCAGATAACGATGCACTGGC	80	M	952
1573217	6498	6517	N/A	N/A	CATTTCTACAAGGTCAGGGA	53	M	953
1573218	6358	6377	N/A	N/A	AAAAAATAACATAATAAGGG	88	M	954
1573259	7721	7740	N/A	N/A	CCCATCACAGAACCTGTTCA	97	M	955
1573265	12519	12538	944	963	CCACTGATGAGGCAGCCCCT	80	M	956
1573285	11738	11757	N/A	N/A	TCCCCCAAGCCCTTGTTTT	105	M	957
1573309	13140	13159	1565	1584	AGAGGCGGCCATAGGGAGGA	72	M	958
1573318	13985	14004	2410	2429	CTCCTCAGCCGGCTCCTGTT	79	M	959
1573331	7895	7914	N/A	N/A	TTATGTAGACTGGTTTTAAA	84	M	960
1573361	5912	5931	N/A	N/A	GAAGGTACCTACCCTAGTCA	70	M	961
1573362	12691	12710	1116	1135	GGCAGGTTCCGTGTCACATG	7	M	962
1573363	14194	14213	N/A	N/A	TGCTTTTCTAAAACACTACA	92	M	963
1573377	13536	13555	1961	1980	GGTAGGACCCTTGAGAAGTG	42	M	964
1573381	14854	14873	N/A	N/A	CCGCTCCCGAATATTTGCC	88	M	965
1573389	5109	5128	N/A	N/A	CTCTCCTCGGCGGGCCCCAC	85	M	966
1573422	9158	9177	N/A	N/A	AGCCTATCCTCCTACTTGGT	90	M	967
1573450	6956	6975	N/A	N/A	TAAGTAAGAACAGGAAAAGA	98	M	968
1573504	5088	5107	N/A	N/A	CCCTGAGCCCCCGGCCCTCA	93	M	969
1573514	13202	13221	1627	1646	GGCGGTGGACTGGGCCCCAG	81	M	970
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	20	M	70
1573589	7809	7828	N/A	N/A	ATCTTAAACAAAAAGCACAA	77	M	971
1573615	6873	6892	N/A	N/A	GCTCGCAGGCTAAATTTTCAG	100	M	972
1573678	15583	15602	3312	3331	AGGGCCGCCACCCTTTCTGC	104	M	973
1573702	12834	12853	1259	1278	GGCCCTTCTCTGGGCCAGGA	97	M	974
1573727	12117	12136	542	561	GCCCCGTCCAAGCTATCCAGA	9*	M	975
1573742	8627	8646	N/A	N/A	GCCTATCTTCTGAACTTTCA	94	M	976
1573761	12423	12442	848	867	GGGCCCCAGGAGGAGCCTGG	102	M	977
1573765	7590	7609	N/A	N/A	AAACTAGCAATGAGAAGCTT	94	M	978
1573770	7462	7481	N/A	N/A	TTTTAGCACCAGCCTACACT	92	M	979
1573800	18449	18468	3934	3953	CCCTCCCCCACTCTCTGTCC	93	M	980
1573822	11868	11887	N/A	N/A	GTCTTGTTTCCCGCCTGTAA	68	M	981
1573831	14070	14089	2495	2514	GACTGGCATGGCTGGGTACA	55	M	982
1510482	10819	10838	363	382	CTGGACTTCTCAGCTTTGCC	28	N	983
1510716	15511	15530	3240	3259	GCTGGCCCAGCTGCCAGCGC	88	N	984
1572331	8787	8806	N/A	N/A	TAAACGGCATGTCCATATTC	16	N	985
1572358	6691	6710	N/A	N/A	CATCTATAGCCCTTCATCT	85	N	986
1572415	6455	6474	N/A	N/A	GAAAGAGGAAAAGGGTTACT	101	N	987
1572431	5290	5309	N/A	N/A	ATTCTGCCTTCGCCCCGAAC	83	N	988

1572456	11892	11911	N/A	N/A	TTCTTGGCTGCTCCCTAGCA	77	N	989
1572483	7874	7893	N/A	N/A	TACTATCAACCAAAAAAAAAA	115	N	990
1572515	7461	7480	N/A	N/A	TTTAGCACCAGCCTACACTC	86	N	991
1572523	5065	5084	N/A	N/A	CAGGCAGAGCCCGCAGTGGG	95	N	992
1572537	6423	6442	N/A	N/A	CTCAAAGAGGAATTCAAGTT	117	N	993
1572562	8618	8637	N/A	N/A	CTGAACCTTCAACTGATGCT	81	N	994
1572568	13430	13449	1855	1874	GTGTGCTGGCCCTGGTGGGT	72	N	995
1572594	13535	13554	1960	1979	GTAGGACCCTTGAGAAGTGG	42	N	996
1572615	6379	6398	N/A	N/A	GAAGCAAAAAGACAACCTCTA	88	N	997
1572617	6579	6598	N/A	N/A	ATAGTATTTCCCTGCATGA	51	N	998
1572646	18448	18467	3933	3952	CCTCCCCACTCTCTGTCCA	104	N	999
1572652	7711	7730	N/A	N/A	AACCTGTTACCAAGTCAGT	97	N	1000
1572657	12518	12537	943	962	CACTGATGAGGCAGCCCCTC	120	N	1001
1572665	12331	12350	756	775	CTAGCCTCTGGCTGTCGAGG	82	N	1002
1572680	14853	14872	N/A	N/A	CGCTCCCGAATATTTGCCCT	103	N	1003
1572707	12113	12132	538	557	GTCCAAGCTATCCAGATCGG	21†	N	1004
1572735	12040	12059	N/A	N/A	TTCTCTTTTCCTTCTGCT	118	N	1005
1572765	13984	14003	2409	2428	TCCTCAGCCGGCTCCTGTTT	117	N	1006
1572781	7413	7432	N/A	N/A	ACAGAGCACCTACTCTGTAT	99	N	1007
1572799	12412	12431	837	856	GGAGCCTGGAACATTCGAGA	7	N	1008
1572802	12833	12852	1258	1277	GCCCTTCTCTGGGCCAGGAG	109	N	1009
1572818	13201	13220	1626	1645	GCGGTGGACTGGGCCCCAGT	82	N	1010
1572854	6990	7009	N/A	N/A	TTGGGAGGAAAGTGAGAACT	104	N	1011
1572859	14477	14496	2619	2638	ACCTTCTCCACCAGGTCGGC	79	N	1012
1572908	13625	13644	2050	2069	GGTAGCCGAAGAGGTGGTGA	69	N	1013
1572916	12690	12709	1115	1134	GCAGGTTCTGGTGTACATGG	9	N	1014
1572932	11981	12000	N/A	N/A	CCTCACAGCACACTGTTGTA	101	N	1015
1572952	8963	8982	N/A	N/A	TGGTATTTTCTTACTGTTTT	15	N	1016
1572984	13664	13683	2089	2108	TGCTGGCGAGGAAGCCACGG	96	N	1017
1573011	5107	5126	N/A	N/A	CTCCTCGCGGGGCCACCC	94	N	1018
1573065	11790	11809	N/A	N/A	TCCAACCTCCCTGTCTTCCAC	99	N	1019
1573104	7031	7050	N/A	N/A	TTACCTTACTTTAAAAAGAA	95	N	1020
1573120	7894	7913	N/A	N/A	TATGTAGACTGGTTTTAAAA	48	N	1021
1573123	12069	12088	N/A	N/A	CCTGCTGTAGAAAAGGGAAG	121†	N	1022
1573146	5087	5106	N/A	N/A	CCTGAGCCCCCGGCCCTCAG	99	N	1023
1573153	13833	13852	2258	2277	CTGGGCCTGCAGGTGGCGAG	103	N	1024
1573164	6401	6420	N/A	N/A	AGAAAATGAAAGAAAGTGCA	93	N	1025
1573175	16459	16478	N/A	N/A	ACCCAAAGCTACAGGGCCCT	105	N	1026
1573188	7661	7680	N/A	N/A	CACAGGAATGTACCTGAGGA	91	N	1027
1573204	6311	6330	N/A	N/A	AGATGGTGTAACTGAACAG	100	N	1028
1573225	9121	9140	N/A	N/A	GTTTCTCACAGCCAATCCAT	46	N	1029
1573281	7767	7786	N/A	N/A	GTGTATTTTGGCAGCCCTC	21	N	1030
1573288	11935	11954	N/A	N/A	AAGCCCACCTCTTACCATCT	90	N	1031
1573296	9501	9520	N/A	N/A	TGCTCTTCTTCTATACTTT	41	N	1032
1573350	12176	12195	601	620	GCTTCGGTTGTCTGGTCGA	1†	N	1033

1573355	14193	14212	N/A	N/A	GCTTTTCTAAAACACTACAC	78	N	1034
1573415	7641	7660	N/A	N/A	ACACAGCAATCATAGTATGC	73	N	1035
1573416	7616	7635	N/A	N/A	TTTTTTAATCACCTGAAATC	112	N	1036
1573440	7573	7592	N/A	N/A	CTTTGAAGGAGAAAAGCAGT	137	N	1037
1573483	18521	18540	4006	4025	CTTTCTGTCCCCATCCTCGC	84	N	1038
1573499	7552	7571	N/A	N/A	ATAAAAGAACAAGTAATCCT	126	N	1039
1573500	6728	6747	N/A	N/A	GAATCCGGGACCTTCAGAGA	87	N	1040
1573539	6955	6974	N/A	N/A	AAGTAAGAACAGGAAAAGAA	112	N	1041
1573541	6760	6779	N/A	N/A	CAGATAACGATGCACTGGCC	82	N	1042
1573546	7808	7827	N/A	N/A	TCTTAAACAAAAGCACAAC	91	N	1043
1573570	14090	14109	N/A	N/A	GGCCGCTCACCTGGCAGACT	84	N	1044
1573571	11737	11756	N/A	N/A	CCCCAAGCCCTTGTTTTT	119	N	1045
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	13	N	70
1573582	6872	6891	N/A	N/A	CTCGCAGGCTAAATTTTCAGG	56	N	1046
1573598	5341	5360	N/A	N/A	AGCTTTTTCTGAGGCTTC	88	N	1047
1573634	17607	17626	N/A	N/A	CCACCCAAATACCTCCTTTC	110	N	1048
1573636	6497	6516	N/A	N/A	ATTTCTACAAGGTCAGGGAA	92	N	1049
1573666	6357	6376	N/A	N/A	AAAAATAACATAATAAGGGA	112	N	1050
1573682	18776	18795	4261	4280	GTCATATAGATATTTATATA	44	N	1051
1573687	13139	13158	1564	1583	GAGGCGGCCATAGGGAGGAG	101	N	1052
1573691	7483	7502	N/A	N/A	TCTTTCTAGACCTGGGTCAT	86	N	1053
1573780	5900	5919	N/A	N/A	CCTAGTCAAAATAAGCCCAT	85	N	1054
1573801	11767	11786	N/A	N/A	CTCATAACCACCACTTTAAC	87	N	1055
1573826	11867	11886	N/A	N/A	TCTTGTTTCCCGCCTGTAAA	93	N	1056
1573829	7745	7764	N/A	N/A	AGAGAAGGGTGTCCATCTCC	86	N	1057
1573840	6823	6842	N/A	N/A	GGACCTGCCAGACTAACAAA	89	N	1058
1573855	14069	14088	2494	2513	ACTGGCATGGCTGGGTACAT	54	N	1059
1572349	9117	9136	N/A	N/A	CTCACAGCCAATCCATCCGT	62	O	1060
1572359	11980	11999	N/A	N/A	CTCACAGCACACTGTTGTAC	98	O	1061
1572370	11891	11910	N/A	N/A	TCTTGCTGCTCCCTAGCAG	102	O	1062
1572393	12039	12058	N/A	N/A	TCTCTTTTCCTTTCCTGCTT	150	O	1063
1572402	7660	7679	N/A	N/A	ACAGGAATGTACCTGAGGAA	67	O	1064
1572417	7551	7570	N/A	N/A	TAAAAGAACAAGTAATCCTG	84	O	1065
1572468	5747	5766	N/A	N/A	AGGTGCTCAATTCTCCATT	37	O	1066
1572470	18445	18464	3930	3949	CCCCACTCTCTGTCCAGCT	74	O	1067
1572494	5039	5058	N/A	N/A	GGATTGGGAAAATAACAAAT	88	O	1068
1572504	6454	6473	N/A	N/A	AAAGAGGAAAAGGGTACTC	109	O	1069
1572557	16450	16469	N/A	N/A	TACAGGGCCCTTTCTAGAAA	75	O	1070
1572575	11934	11953	N/A	N/A	AGCCACCTCTTACCATCTG	97	O	1071
1572590	7807	7826	N/A	N/A	CTTAAACAAAAGCACAACA	102	O	1072
1572611	12517	12536	942	961	ACTGATGAGGCAGCCCCTCC	77	O	1073
1572616	14845	14864	N/A	N/A	AATATTTGCCCTTCTTGGA	100	O	1074
1572623	14068	14087	2493	2512	CTGGCATGGCTGGGTACATC	36	O	1075
1572638	18775	18794	4260	4279	TCATATAGATATTTATATAT	89	O	1076
1572659	6496	6515	N/A	N/A	TTTCTACAAGGTCAGGGAAG	87	O	1077

1572674	8273	8292	N/A	N/A	GCCAACTAGTTTTCTTTTTT	35	O	1078
1572698	5106	5125	N/A	N/A	TCCTCGGCGGGCCCCACCCC	101	O	1079
1572703	14192	14211	N/A	N/A	CTTTTCTAAAACACTACACC	93	O	1080
1572755	6759	6778	N/A	N/A	AGATAACGATGCACTGGCCT	81	O	1081
1572770	11736	11755	N/A	N/A	CCCCAAGCCCTTGGTTTTTA	97	O	1082
1572777	5340	5359	N/A	N/A	GCTTTTTCCTGGAGGCTTCA	106	O	1083
1572813	11866	11885	N/A	N/A	CTTGTTTCCCGCCTGTAAAA	76	O	1084
1572844	6952	6971	N/A	N/A	TAAGAACAGGAAAAGAAATT	109	O	1085
1572852	7572	7591	N/A	N/A	TTTGAAGGAGAAAAGCAGTC	101	O	1086
1572870	13138	13157	1563	1582	AGGCGGCCATAGGGAGGAGG	101	O	1087
1572874	11789	11808	N/A	N/A	CCAACCTCCCTGTCTTCCACC	75	O	1088
1572907	6310	6329	N/A	N/A	GATGGTGTAACCTGAACAGA	93	O	1089
1572919	7030	7049	N/A	N/A	TACCTTACTTTAAAAAGAAA	108	O	1090
1572960	9499	9518	N/A	N/A	CTCTTCTTCTATACTTTGC	19	O	1091
1572977	13428	13447	1853	1872	GTGCTGGCCCTGGTGGGTAG	73	O	1092
1572990	8786	8805	N/A	N/A	AAACGGCATGTCCATATTCT	52	O	1093
1573004	15292	15311	3021	3040	GCTTCCCCTTCCCTCTCCCG	73	O	1094
1573029	7893	7912	N/A	N/A	ATGTAGACTGGTTTTAAAT	40	O	1095
1573062	5288	5307	N/A	N/A	TCTGCCCTCGCCCGGAACCC	51	O	1096
1573068	8955	8974	N/A	N/A	TCTTACTGTTTTCTTCTTT	34	O	1097
1573095	7743	7762	N/A	N/A	AGAAGGGTGTCCATCTCCCT	127	O	1098
1573100	7640	7659	N/A	N/A	CACAGCAATCATAGTATGCC	87	O	1099
1573122	6822	6841	N/A	N/A	GACCTGCCAGACTAACAAC	84	O	1100
1573134	13534	13553	1959	1978	TAGGACCCTTGAGAAGTGGA	32	O	1101
1573140	6989	7008	N/A	N/A	TGGGAGGAAAGTGAGAACTA	74	O	1102
1573180	6378	6397	N/A	N/A	AAGCAAAAAGACAACCTCTAC	76	O	1103
1573192	11766	11785	N/A	N/A	TCATAACCACCACTTTAACC	98	O	1104
1573211	13832	13851	2257	2276	TGGGCTGCAGGTGGCGAGG	128	O	1105
1573215	12330	12349	755	774	TAGCCTCTGGCTGTGAGGG	77	O	1106
1573234	18520	18539	4005	4024	TTTCTGTCCCCATCCTCGCC	91	O	1107
1573255	10706	10725	N/A	N/A	CCTCATTGACATCTACAGGA	98	O	1108
1573260	12689	12708	1114	1133	CAGGTTTCGGTGTACATGGG	7	O	1109
1573270	17606	17625	N/A	N/A	CACCCAAATACCTCCTTTCT	93	O	1110
1573283	12111	12130	536	555	CCAAGCTATCCAGATCGGAG	25†	O	1111
1573289	7615	7634	N/A	N/A	TTTTTAATCACCTGAAATCT	66	O	1112
1573304	12068	12087	N/A	N/A	CTGCTGTAGAAAAGGGAAGA	83†	O	1113
1573317	7458	7477	N/A	N/A	AGCACCAGCCTACACTCCTA	54	O	1114
1573323	12832	12851	1257	1276	CCCTTCTCTGGGCCAGGAGG	102	O	1115
1573333	6871	6890	N/A	N/A	TCGCAGGCTAAATTCAGGA	19	O	1116
1573339	6422	6441	N/A	N/A	TCAAAGAGGAATTCAAGTTT	112	O	1117
1573414	12410	12429	835	854	AGCCTGGAACATTCGAGATG	67	O	1118
1573452	7766	7785	N/A	N/A	TGTATTTTTGCCAGCCCTCC	40	O	1119
1573458	13620	13639	2045	2064	CCGAAGAGGTGGTGACCGTA	46	O	1120
1573507	13198	13217	1623	1642	GTGGACTGGGCCCCAGTAGA	67	O	1121
1573573	6356	6375	N/A	N/A	AAAATAACATAATAAGGGAG	77	O	1122

1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	12	O	70
1573616	13983	14002	2408	2427	CCTCAGCCGGCTCCTGTTTG	86	O	1123
1573638	7412	7431	N/A	N/A	CAGAGCACCTACTCTGTATC	84	O	1124
1573647	7873	7892	N/A	N/A	ACTATCAACCAAAAAAAAAAA	109	O	1125
1573661	6690	6709	N/A	N/A	ATCTATAGCCCCCTTCATCTT	106	O	1126
1573688	7481	7500	N/A	N/A	TTTCTAGACCTGGGTCATGT	95	O	1127
1573720	6558	6577	N/A	N/A	GCTGTTTCACAGCCCTCTGT	47	O	1128
1573729	14286	14305	N/A	N/A	GTGCTTGTAGCCCCCGCCTC	67	O	1129
1573766	14089	14108	N/A	N/A	GCCGCTCACCTGGCAGACTG	88	O	1130
1573808	12175	12194	600	619	CTTCGGTTGTCCTGGTCGAT	4†	O	1131
1573830	13663	13682	2088	2107	GCTGGCGAGGAAGCCACGGT	81	O	1132
1573834	6400	6419	N/A	N/A	GAAAATGAAAGAAAGTGCAA	100	O	1133
1573839	5086	5105	N/A	N/A	CTGAGCCCCCGGCCCTCAGG	88	O	1134
1573850	6727	6746	N/A	N/A	AATCCGGGACCTTCAGAGAG	69	O	1135
1573860	7709	7728	N/A	N/A	CCTGTTACCAAGTCAGTTA	69	O	1136
1475477	8784	8803	N/A	N/A	ACGGCATGTCCATATTCTGT	46	P	150
1572333	11765	11784	N/A	N/A	CATAACCACCACTTTAACCA	101	P	1137
1572348	18519	18538	4004	4023	TTCTGTCCCCATCCTCGCCA	60	P	1138
1572353	11735	11754	N/A	N/A	CCCAAGCCCTTGGTTTTTAT	100	P	1139
1572371	7892	7911	N/A	N/A	TGTAGACTGGTTTTAAAATA	54	P	1140
1572381	6556	6575	N/A	N/A	TGTTTCACAGCCCTCTGTCC	63	P	1141
1572430	11890	11909	N/A	N/A	CTTGGCTGCTCCCTAGCAGC	96	P	1142
1572440	13662	13681	2087	2106	CTGGCGAGGAAGCCACGGTG	94	P	1143
1572473	12067	12086	N/A	N/A	TGCTGTAGAAAAGGGAAGAC	100†	P	1144
1572488	16446	16465	N/A	N/A	GGGCCCTTTCTAGAAAGTTA	72	P	1145
1572513	6399	6418	N/A	N/A	AAAATGAAAGAAAGTGCAAA	87	P	1146
1572541	6421	6440	N/A	N/A	CAAAGAGGAATTCAAGTTTT	81	P	1147
1572553	13411	13430	1836	1855	TAGGGCCTCAGAGACCCCAG	103	P	1148
1572578	6495	6514	N/A	N/A	TTCTACAAGGTCAGGGAAGA	90	P	1149
1572584	9498	9517	N/A	N/A	TCTTTCTTCTATACTTTGCT	21	P	1150
1572587	5745	5764	N/A	N/A	GTTGCTCAATTCTCCATTTT	49	P	1151
1572597	12110	12129	535	554	CAAGCTATCCAGATCGGAGG	36†	P	1152
1572599	18769	18788	4254	4273	AGATATTTATATATATAAAT	108	P	1153
1572613	13982	14001	2407	2426	CTCAGCCGGCTCCTGTTTGA	97	P	1154
1572653	12516	12535	941	960	CTGATGAGGCAGCCCCTCCC	103	P	1155
1572656	7549	7568	N/A	N/A	AAAGAACAAGTAATCCTGGG	69	P	1156
1572733	13136	13155	1561	1580	GCGGCCATAGGGAGGAGGTG	93	P	1157
1572747	14191	14210	N/A	N/A	TTTTCTAAAACACTACACCA	104	P	1158
1572748	14283	14302	N/A	N/A	CTTGTAAGCCCCCGCTCAAA	72	P	1159
1572752	6377	6396	N/A	N/A	AGCAAAAAGACAACCTCTACA	68	P	1160
1572760	11933	11952	N/A	N/A	GCCCACCTCTTACCATCTGG	121	P	1161
1572797	11788	11807	N/A	N/A	CAACTCCCTGTCTTCCACCA	95	P	1162
1572809	13815	13834	2240	2259	AGGTTCCCTCGATAGCCCGGT	79	P	1163
1572810	12290	12309	715	734	GGAAGGAGGAAAGAGTGAG	64	P	1164
1572819	14067	14086	2492	2511	TGGCATGGCTGGGTACATCT	22	P	1165

1572876	6868	6887	N/A	N/A	CAGGCTAAATTTTCAGGATCA	62	P	1166
1572878	7613	7632	N/A	N/A	TTTAATCACCTGAAATCTGA	92	P	1167
1572947	12831	12850	1256	1275	CCTTCTCTGGGCCAGGAGGA	97	P	1168
1572971	6951	6970	N/A	N/A	AAGAACAGGAAAAGAAATTA	112	P	1169
1572993	7571	7590	N/A	N/A	TTGAAGGAGAAAAGCAGTCA	85	P	1170
1573048	17586	17605	N/A	N/A	GCCCTTTTCTCATTGGAGCT	90	P	1171
1573117	7637	7656	N/A	N/A	AGCAATCATAGTATGCCCTT	38	P	1172
1573137	7765	7784	N/A	N/A	GTATTTTGTCCAGCCCTCCT	28	P	1173
1573148	6689	6708	N/A	N/A	TCTATAGCCCCTTCATCTTA	95	P	1174
1573151	7806	7825	N/A	N/A	TTAAACAAAAAGCACAAACAA	93	P	1175
1573159	7025	7044	N/A	N/A	TACTTTAAAAAGAAAATGAT	141	P	1176
1573183	13618	13637	2043	2062	GAAGAGGTGGTGACCGTAGG	82	P	1177
1573186	18410	18429	3895	3914	CTGAGCAGCACCCCTCTTGGC	83	P	1178
1573202	11979	11998	N/A	N/A	TCACAGCACACTGTTGTACT	105	P	1179
1573207	12407	12426	832	851	CTGGAACATTTCGAGATGTGG	21	P	411
1573240	6974	6993	N/A	N/A	AACTAGAAAAAGAGCCCCTA	105	P	1180
1573272	7740	7759	N/A	N/A	AGGGTGTCCATCTCCCTTCC	92	P	1181
1573278	12174	12193	599	618	TTCGGTTGTCCTGGTCGATA	2 ⁺	P	1182
1573297	10665	10684	N/A	N/A	CTGTTCTTTACATTGCACCT	82	P	1183
1573298	5105	5124	N/A	N/A	CCTCGGCGGGCCCCACCCCC	120	P	1184
1573322	5337	5356	N/A	N/A	TTTTCTGGAGGCTTCATGC	74	P	1185
1573332	13197	13216	1622	1641	TGGACTGGGCCCCAGTAGAG	52	P	1186
1573359	7411	7430	N/A	N/A	AGAGCACCTACTCTGTATCT	50	P	1187
1573364	8954	8973	N/A	N/A	CTTACTGTTTTCTTCCTTTC	35	P	1188
1573367	6355	6374	N/A	N/A	AAATAACATAATAAGGGAGG	96	P	1189
1573376	12038	12057	N/A	N/A	CTCTTTTCCTTTCTCTGCTTC	116	P	1190
1573399	9111	9130	N/A	N/A	GCCAATCCATCCGTATCTGT	15	P	1191
1573418	6726	6745	N/A	N/A	ATCCGGGACCTTCAGAGAGG	82	P	1192
1573423	14088	14107	N/A	N/A	CCGCTCACCTGGCAGACTGA	34	P	1193
1573432	15289	15308	3018	3037	TCCCGTTCCTCTCCCGGGC	74	P	1194
1573435	11865	11884	N/A	N/A	TTGTTTCCCGCCTGTAAAAC	88	P	1195
1573505	7659	7678	N/A	N/A	CAGGAATGTACCTGAGGAAC	65	P	1196
1573531	6758	6777	N/A	N/A	GATAACGATGCACTGGCCTA	89	P	1197
1573543	12643	12662	1068	1087	GGTAGGTTCCCACCACCCAC	86	P	1198
1573567	6821	6840	N/A	N/A	ACCTGCCAGACTAACAAACC	79	P	1199
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	15	P	70
1573584	13533	13552	1958	1977	AGGACCCTTGAGAAGTGGA	31	P	1200
1573585	6309	6328	N/A	N/A	ATGGTGTAACCTGAACAGAA	100	P	1201
1573586	7708	7727	N/A	N/A	CTGTTACCAAGTCAGTTAG	57	P	1202
1573597	14822	14841	N/A	N/A	ACAGGTAGTCCCATCTGAGC	68	P	1203
1573606	7844	7863	N/A	N/A	AAGAACAACACCCACCATAG	101	P	1204
1573620	7457	7476	N/A	N/A	GCACCAGCCTACACTCCTAG	31	P	1205
1573623	8232	8251	N/A	N/A	GATGGATCTTTGCTCTTGTT	27	P	1206
1573641	5287	5306	N/A	N/A	CTGCCTTCGCCCCGAACCCC	68	P	1207
1573671	7480	7499	N/A	N/A	TTCTAGACCTGGGTCATGTT	61	P	1208

1573677	5038	5057	N/A	N/A	GATTGGGAAAATAACAAATG	100	P	1209
1573744	5085	5104	N/A	N/A	TGAGCCCCCGGCCCTCAGGC	51	P	1210
1573836	6453	6472	N/A	N/A	AAGAGGAAAAGGGTTACTCA	94	P	1211
1510542	10501	10520	192	211	CCATTCTCCTCTGCCTGGGC	78	Q	1212
1572360	14189	14208	N/A	N/A	TTCTAAAACACTACACCAGC	87	Q	1213
1572388	6950	6969	N/A	N/A	AGAACAGGAAAAGAAATTAA	93	Q	1214
1572391	9109	9128	N/A	N/A	CAATCCATCCGTATCTGTCT	58	Q	1215
1572395	8953	8972	N/A	N/A	TTACTGTTTTCTTCCTTTCC	47	Q	1216
1572396	6668	6687	N/A	N/A	CAATGAAGCCCAGGCTCAA	100	Q	1217
1572407	16433	16452	N/A	N/A	AAAGTTACAGATCTAGAGAT	114	Q	1218
1572408	12289	12308	714	733	GAAGGAGGAAAGAGTGAGG	108	Q	1219
1572438	14281	14300	N/A	N/A	TGTAGCCCCCGCCTCAAAAC	85	Q	1220
1572449	13617	13636	2042	2061	AAGAGGTGGTGACCGTAGGC	66	Q	1221
1572452	12109	12128	534	553	AAGCTATCCAGATCGGAGGG	54†	Q	1222
1572500	6491	6510	N/A	N/A	ACAAGGTCAGGGAAGAAGGC	71	Q	1223
1572505	6308	6327	N/A	N/A	TGGTGTAACCTGAACAGAAG	84	Q	1224
1572531	12830	12849	1255	1274	CTTCTCTGGGCCAGGAGGAA	111	Q	1225
1572548	14821	14840	N/A	N/A	CAGGTAGTCCCATCTGAGCA	93	Q	1226
1572572	12037	12056	N/A	N/A	TCTTTTCCTTTCCTGCTTCC	131	Q	1227
1572619	7612	7631	N/A	N/A	TTAATCACCTGAAATCTGAT	101	Q	1228
1572627	15288	15307	3017	3036	CCCGTTCCCTCTCCCGGGCA	60	Q	1229
1572684	11764	11783	N/A	N/A	ATAACCACCACTTTAACCAT	108	Q	1230
1572700	13814	13833	2239	2258	GGTTCCTCGATAGCCCGGTG	59	Q	1231
1572726	7739	7758	N/A	N/A	GGGTGTCCATCTCCCTTCCC	119	Q	1232
1572746	11932	11951	N/A	N/A	CCCACCTCTTACCATCTGGG	94	Q	1233
1572759	6354	6373	N/A	N/A	AATAACATAATAAGGGAGGT	103	Q	1234
1572761	6820	6839	N/A	N/A	CCTGCCAGACTAACAACCA	80	Q	1235
1572769	18408	18427	3893	3912	GAGCAGCACCTCTTGCTC	99	Q	1236
1572775	17576	17595	N/A	N/A	CATTGGAGCTGCCTACCCCA	88	Q	1237
1572803	5104	5123	N/A	N/A	CTCGGCGGGCCCCACCCCT	82	Q	1238
1572807	6420	6439	N/A	N/A	AAAGAGGAATTCAAGTTTAA	116	Q	1239
1572817	13980	13999	2405	2424	CAGCCGGCTCCTGTTTGATC	95	Q	1240
1572821	6867	6886	N/A	N/A	AGGCTAAATTTAGGATCAT	47	Q	1241
1572826	7843	7862	N/A	N/A	AGAACAACACCCACCATAGC	111	Q	1242
1572837	5285	5304	N/A	N/A	GCCTTCGCCCCGAACCCAC	68	Q	1243
1572847	9495	9514	N/A	N/A	TTCTTCTATACTTTGCTGTA	39	Q	1244
1572857	13532	13551	1957	1976	GGACCCCTGAGAAGTGGAAG	40	Q	1245
1572884	6757	6776	N/A	N/A	ATAACGATGCACTGGCCTAA	106	Q	1246
1572890	11972	11991	N/A	N/A	ACACTGTTGTACTGTGATGT	91	Q	1247
1572937	7707	7726	N/A	N/A	TGTTACCAAGTCAGTTAGG	44	Q	1248
1572970	18518	18537	4003	4022	TCTGTCCCCATCCTCGCCAC	74	Q	1249
1572995	13135	13154	1560	1579	CGGCCATAGGGAGGAGGTGG	93	Q	1250
1573017	7410	7429	N/A	N/A	GAGCACCTACTCTGTATCTG	27	Q	1251
1573025	12066	12085	N/A	N/A	GCTGTAGAAAAGGGAAGACT	105†	Q	1252
1573072	12515	12534	940	959	TGATGAGGCAGCCCCTCCCC	85	Q	1253

1573073	13407	13426	1832	1851	GCCTCAGAGACCCCAGGGAG	74	Q	1254
1573078	7022	7041	N/A	N/A	TTTAAAAAGAAAATGATTAA	87	Q	1255
1573079	11832	11851	N/A	N/A	CAAGGATCCATCTCAAGCAC	109	Q	1256
1573090	6397	6416	N/A	N/A	AATGAAAGAAAGTGCAAAGA	100	Q	1257
1573097	12642	12661	1067	1086	GTAGGTTCCACCACCCACT	91	Q	1258
1573105	14087	14106	N/A	N/A	CGCTCACCTGGCAGACTGAC	79	Q	1259
1573121	7891	7910	N/A	N/A	GTAGACTGGTTTTAAAATAC	31	Q	1260
1573131	13661	13680	2086	2105	TGGCGAGGAAGCCACGGTGG	83	Q	1261
1573145	7636	7655	N/A	N/A	GCAATCATAGTATGCCCTTC	19	Q	1262
1573222	7570	7589	N/A	N/A	TGAAGGAGAAAAGCAGTCAT	83	Q	1263
1573224	5336	5355	N/A	N/A	TTTCCTGGAGGCTTCATGCC	75	Q	1264
1573246	7527	7546	N/A	N/A	TAAGGAGTGGCAGACGAGGA	90	Q	1265
1573258	7456	7475	N/A	N/A	CACCAGCCTACACTCCTAGC	81	Q	1266
1573269	6555	6574	N/A	N/A	GTTTCACAGCCCTCTGTCCT	82	Q	1267
1573358	13196	13215	1621	1640	GGACTGGGCCCCAGTAGAGG	83	Q	1268
1573380	11719	11738	N/A	N/A	TTATACCACTTCTGGCCGGG	99	Q	1269
1573456	6722	6741	N/A	N/A	GGGACCTTCAGAGAGGCCTC	83	Q	1270
1573482	5084	5103	N/A	N/A	GAGCCCCCGGCCCTCAGGCC	100	Q	1271
1573510	7658	7677	N/A	N/A	AGGAATGTACCTGAGGAACA	84	Q	1272
1573513	6376	6395	N/A	N/A	GCAAAAAGACAACCTCTACAA	93	Q	1273
1573523	6452	6471	N/A	N/A	AGAGGAAAAGGGTTACTCAA	109	Q	1274
1573562	5037	5056	N/A	N/A	ATTGGGAAAATAACAAATGG	81	Q	1275
1573563	8783	8802	N/A	N/A	CGGCATGTCCATATTCTGTA	30	Q	1276
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	24	Q	70
1573581	12173	12192	598	617	TCGGTTGTCCTGGTCGATAT	13†	Q	1277
1573653	5744	5763	N/A	N/A	TTGCTCAATTCTCCATTTCC	71	Q	1278
1573659	14066	14085	2491	2510	GGCATGGCTGGGTACATCTA	22	Q	190
1573662	7479	7498	N/A	N/A	TCTAGACCTGGGTCTATGTTT	92	Q	1279
1573667	11786	11805	N/A	N/A	ACTCCCTGTCTTCCACCATC	90	Q	1280
1573693	6972	6991	N/A	N/A	CTAGAAAAAGAGCCCCTAAG	106	Q	1281
1573697	11889	11908	N/A	N/A	TTGGCTGCTCCCTAGCAGCC	110	Q	1282
1573698	8231	8250	N/A	N/A	ATGGATCTTTGCTCTTGTTTC	39	Q	1283
1573776	18768	18787	4253	4272	GATATTTATATATATAAATT	97	Q	1284
1573783	7764	7783	N/A	N/A	TATTTTGGCCAGCCCTCCTA	77	Q	1285
1573798	12406	12425	831	850	TGGAACATTTCGAGATGTGGG	6	Q	1286
1573837	7805	7824	N/A	N/A	TAAACAAAAAGCACAACAAA	87	Q	1287
1475572	5742	5761	N/A	N/A	GCTCAATTCTCCATTTCCAT	11	R	870
1572392	9102	9121	N/A	N/A	TCCGTATCTGTCTATCAGCA	31	R	1288
1572418	6659	6678	N/A	N/A	CCAGGCTCAAAGAGAAGTGA	86	R	1289
1572442	12288	12307	713	732	AAGGAGGAAAGAGTGGAGGT	72	R	1290
1572444	11831	11850	N/A	N/A	AAGGATCCATCTCAAGCACC	61	R	1291
1572496	13165	13184	1590	1609	CCTGGATGGGCATTGCTGTT	48	R	1292
1572507	7657	7676	N/A	N/A	GGAATGTACCTGAGGAACAC	60	R	1293
1572511	13334	13353	1759	1778	GGGAAATGCTCCAGGAGGAG	44	R	1294
1572512	6419	6438	N/A	N/A	AAGAGGAATTCAAGTTTTAG	87	R	1295

1572534	7706	7725	N/A	N/A	GTTACCAAGTCAGTTAGGT	12	R	227
1572543	8782	8801	N/A	N/A	GGCATGTCCATATTCTGTAG	52	R	1296
1572544	8951	8970	N/A	N/A	ACTGTTTTCTTCCTTTCCAC	31	R	1297
1572574	6756	6775	N/A	N/A	TAACGATGCACTGGCCTAAG	62	R	1298
1572580	12108	12127	533	552	AGCTATCCAGATCGGAGGGA	43†	R	1299
1572663	7478	7497	N/A	N/A	CTAGACCTGGGTCATGTTTT	57	R	1300
1572671	7890	7909	N/A	N/A	TAGACTGGTTTTTAAAATACT	68	R	1301
1572696	11763	11782	N/A	N/A	TAACCACCACTTTAACCATC	77	R	1302
1572716	18517	18536	4002	4021	CTGTCCCCATCCTCGCCACC	108	R	1303
1572723	6949	6968	N/A	N/A	GAACAGGAAAAGAAATTAAG	98	R	1304
1572731	6375	6394	N/A	N/A	CAAAAAGACAACCTCTACAAA	105	R	1305
1572742	12172	12191	597	616	CGGTTGTCCTGGTCGATATC	3‡	R	1306
1572749	11969	11988	N/A	N/A	CTGTTGTACTGTGATGTGGT	78	R	1307
1572764	14279	14298	N/A	N/A	TAGCCCCCGCCTCAAAACCA	93	R	1308
1572801	7763	7782	N/A	N/A	ATTTTTGCCAGCCCTCCTAG	57	R	1309
1572805	5036	5055	N/A	N/A	TTGGGAAAATAACAAATGGA	72	R	1310
1572832	6721	6740	N/A	N/A	GGACCTTCAGAGAGGCCTCA	95	R	1311
1572863	6353	6372	N/A	N/A	ATAACATAATAAGGAGGTA	87	R	1312
1572881	6971	6990	N/A	N/A	TAGAAAAAGAGCCCCTAAGT	69	R	1313
1572898	6450	6469	N/A	N/A	AGGAAAAGGGTTACTCAAGA	106	R	1314
1572924	12978	12997	1403	1422	GGGAGGCAGAGGAAGAGGAG	81	R	1315
1572935	13813	13832	2238	2257	GTTCTCGATAGCCCGGTGG	44	R	1316
1572959	5284	5303	N/A	N/A	CCTTCGCCCAGAACCCCACT	85	R	1317
1572978	7455	7474	N/A	N/A	ACCAGCCTACACTCCTAGCA	61	R	1318
1572979	7569	7588	N/A	N/A	GAAGGAGAAAAGCAGTCATA	69	R	1319
1572982	12829	12848	1254	1273	TTCTCTGGGCCAGGAGGAAG	86	R	1320
1573056	15198	15217	2927	2946	CGTAGAATGGATGGTTGCGA	29	R	1321
1573074	5103	5122	N/A	N/A	TCGGCGGGCCCCACCCCCTG	84	R	1322
1573109	16408	16427	N/A	N/A	AAAACATGAAAGACCTCGCA	98	R	1323
1573115	10473	10492	164	183	ACAGAAACTTCTCTGCTCCA	51	R	1324
1573142	7804	7823	N/A	N/A	AAACAAAAAGCACAAACAAAG	88	R	1325
1573147	13524	13543	1949	1968	GAGAAGTGGAAGAGGAAGAG	64	R	1326
1573184	18407	18426	3892	3911	AGCAGCACCTCTTGGCTCT	94	R	1327
1573185	5083	5102	N/A	N/A	AGCCCCCGGCCCTCAGGCCA	80	R	1328
1573191	6865	6884	N/A	N/A	GCTAAATTTACAGGATCATTG	36	R	1329
1573254	13660	13679	2085	2104	GGCGAGGAAGCCACGGTGGC	85	R	1330
1573277	14065	14084	2490	2509	GCATGGCTGGGTACATCTAC	27	R	1331
1573280	7611	7630	N/A	N/A	TAATCACCTGAAATCTGATA	99	R	1332
1573329	13979	13998	2404	2423	AGCCGGCTCCTGTTTGATCT	85	R	1333
1573341	11888	11907	N/A	N/A	TGGCTGCTCCCTAGCAGCCA	90	R	1334
1573345	12036	12055	N/A	N/A	CTTTTCCTTTCTGCTTCCC	99	R	1335
1573346	17575	17594	N/A	N/A	ATTGGAGCTGCCTACCCCAA	84	R	1336
1573360	7409	7428	N/A	N/A	AGCACCTACTCTGTATCTGG	24	R	1337
1573371	18760	18779	4245	4264	TATATATAAATTATTAGTGT	92	R	1338
1573427	6554	6573	N/A	N/A	TTTACAGCCCTCTGTCCTG	74	R	1339

1573436	7021	7040	N/A	N/A	TTAAAAAGAAAATGATTAAG	88	R	1340
1573466	6307	6326	N/A	N/A	GGTGTAACTGAACAGAAGC	83	R	1341
1573479	7925	7944	N/A	N/A	CTACAGCTATTTTCCCACAT	39	R	1342
1573521	12599	12618	1024	1043	GGGAGCACCCTAGCCCCAG	88	R	1343
1573528	6396	6415	N/A	N/A	ATGAAAGAAAGTGCAAAGAA	100	R	1344
1573529	12065	12084	N/A	N/A	CTGTAGAAAAGGGAAGACTC	106	R	1345
1573530	7635	7654	N/A	N/A	CAATCATAGTATGCCCTTCT	26	R	1346
1573533	14188	14207	N/A	N/A	TCTAAAACACTACACCAGCG	68	R	1347
1573542	11708	11727	N/A	N/A	CTGGCCGGGCACAGAGGCTT	83	R	1348
1573568	7738	7757	N/A	N/A	GGTGTCCATCTCCCTTCCCC	74	R	1349
1573575	7842	7861	N/A	N/A	GAACAACACCCACCATAGCA	73	R	1350
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	24	R	70
1573605	14810	14829	N/A	N/A	ATCTGAGCATGCCTTTTCCC	64	R	1351
1573617	12377	12396	802	821	GGGAGCATGATATCCAGTGG	18	R	21
1573622	11914	11933	N/A	N/A	GGGATTTCTCACTTTCCTCA	88	R	1352
1573625	5335	5354	N/A	N/A	TTCTTGAGGCTTCATGCCC	66	R	1353
1573639	6819	6838	N/A	N/A	CTGCCAGACTAACAAACCAG	68	R	1354
1573716	12514	12533	939	958	GATGAGGCAGCCCCTCCCC	100	R	1355
1573728	13616	13635	2041	2060	AGAGGTGGTGACCGTAGGCA	27	R	1356
1573737	11785	11804	N/A	N/A	CTCCCTGTCTTCCACCATCT	78	R	1357
1573746	7526	7545	N/A	N/A	AAGGAGTGGCAGACGAGGAA	83	R	1358
1573767	9486	9505	N/A	N/A	ACTTTGCTGTATTCTCCTCA	47	R	1359
1573816	14086	14105	N/A	N/A	GCTCACCTGGCAGACTGACT	64	R	1360
1573838	6490	6509	N/A	N/A	CAAGGTCAGGGAAGAAGGCC	57	R	1361
1572361	5283	5302	N/A	N/A	CTTCGCCCCGAACCCCACTC	104	S	1362
1572363	10459	10478	150	169	GCTCCACCCCAAGTTCCCCA	87	S	1363
1572373	11912	11931	N/A	N/A	GATTTCTCACTTTCCTCACA	94	S	1364
1572377	11953	11972	N/A	N/A	TGGTGAGTACTCTTGCTCAA	100	S	1365
1572428	11266	11285	N/A	N/A	GCTCTAAGAATCTCTCTGGC	97	S	1366
1572429	7634	7653	N/A	N/A	AATCATAGTATGCCCTTCTT	42	S	1367
1572467	18515	18534	4000	4019	GTCCCCATCCTCGCCACCTC	112	S	1368
1572476	12474	12493	899	918	CAGACAAAACCTCCACCAGTG	52	S	1369
1572519	14186	14205	N/A	N/A	TAAAACACTACACCAGCGCA	104	S	1370
1572552	13158	13177	1583	1602	GGGCATTGCTGTTGGCTAAG	30	S	1371
1572566	5102	5121	N/A	N/A	CGGCGGGCCCCACCCCTGA	115	S	1372
1572609	7924	7943	N/A	N/A	TACAGCTATTTTCCCACATT	73	S	1373
1572639	7454	7473	N/A	N/A	CCAGCCTACACTCCTAGCAG	73	S	1374
1572640	6970	6989	N/A	N/A	AGAAAAAGAGCCCCTAAGTA	107	S	1375
1572661	12171	12190	596	615	GGTTGTCCTGGTCGATATCC	6 ⁺	S	1376
1572669	7762	7781	N/A	N/A	TTTTTGCCAGCCCTCCTAGA	91	S	1377
1572688	6948	6967	N/A	N/A	AACAGGAAAAGAAATTAAGA	99	S	1378
1572693	13513	13532	1938	1957	GAGGAAGAGTTGGAAGAGGA	67	S	1379
1572706	7803	7822	N/A	N/A	AACAAAAAGCACAACAAAGA	108	S	1380
1572724	11762	11781	N/A	N/A	AACCACCACTTTAACCATCC	102	S	1381
1572739	13659	13678	2084	2103	GCGAGGAAGCCACGGTGGCA	81	S	1382

1572741	14064	14083	2489	2508	CATGGCTGGGTACATCTACC	51	S	112
1572758	7656	7675	N/A	N/A	GAATGTACCTGAGGAACACA	83	S	1383
1572791	7020	7039	N/A	N/A	TAAAAAGAAAATGATTAAGA	113	S	1384
1572794	8781	8800	N/A	N/A	GCATGTCCATATTCTGTAGT	42	S	1385
1572824	14278	14297	N/A	N/A	AGCCCCCGCCTCAAAACCAC	108	S	1386
1572825	8950	8969	N/A	N/A	CTGTTTTCTTCCTTTCCACT	45	S	1387
1572842	7477	7496	N/A	N/A	TAGACCTGGGTCATGTTTTA	96	S	1388
1572848	12596	12615	1021	1040	AGCACCACTAGCCCCAGAGC	88	S	1389
1572875	7705	7724	N/A	N/A	TTCACCAAGTCAGTTAGGTT	39	S	1390
1572883	5035	5054	N/A	N/A	TGGGAAAATAACAAATGGAG	77	S	1391
1572905	6815	6834	N/A	N/A	CAGACTAACAAACCAGTCCA	94	S	1392
1572930	6418	6437	N/A	N/A	AGAGGAATTCAAGTTTTAGA	113	S	1393
1572933	6306	6325	N/A	N/A	GTGTAACCTGAACAGAAGCG	74	S	1394
1572965	13812	13831	2237	2256	TTCCTCGATAGCCCGGTGGG	94	S	1395
1572974	12977	12996	1402	1421	GGAGGCAGAGGAAGAGGAGG	98	S	1396
1573005	6864	6883	N/A	N/A	CTAAATTTTCAGGATCATTGG	80	S	1397
1573021	7568	7587	N/A	N/A	AAGGAGAAAAGCAGTCATAA	83	S	1398
1573024	6755	6774	N/A	N/A	AACGATGCACTGGCCTAAGC	74	S	1399
1573031	13978	13997	2403	2422	GCCGGCTCCTGTTTGATCTG	93	S	1400
1573041	16058	16077	N/A	N/A	GCAGAGCCAGACCATGTCTC	118	S	1401
1573042	6658	6677	N/A	N/A	CAGGCTCAAAGAGAAGTGAC	99	S	1402
1573057	14085	14104	N/A	N/A	CTCACCTGGCAGACTGACTG	81	S	1403
1573070	13613	13632	2038	2057	GGTGGTGACCGTAGGCACCG	125	S	1404
1573101	11887	11906	N/A	N/A	GGCTGCTCCCTAGCAGCCAG	104	S	1405
1573106	6374	6393	N/A	N/A	AAAAAGACAACCTCTACAAA	121	S	1406
1573128	15196	15215	2925	2944	TAGAATGGATGGTTGCGATT	46	S	1407
1573154	6449	6468	N/A	N/A	GGAAAAGGGTTACTCAAGAA	92	S	1408
1573198	7525	7544	N/A	N/A	AGGAGTGGCAGACGAGGAAA	84	S	1409
1573252	12828	12847	1253	1272	TCTCTGGGCCAGGAGGAAGT	91	S	1410
1573256	7737	7756	N/A	N/A	GTGTCCATCTCCCTTCCCCA	61	S	1411
1573262	7408	7427	N/A	N/A	GCACCTACTCTGTATCTGGC	11	S	1412
1573279	7610	7629	N/A	N/A	AATCACCTGAAATCTGATAA	92	S	1413
1573284	17574	17593	N/A	N/A	TTGGAGCTGCCTACCCCAAC	111	S	1414
1573299	12107	12126	532	551	GCTATCCAGATCGGAGGGAG	44†	S	1415
1573315	12376	12395	801	820	GGAGCATGATATCCAGTGGG	9	S	410
1573335	18211	18230	N/A	N/A	CCTTGCCCCCTCTTACCGAA	107	S	1416
1573348	9480	9499	N/A	N/A	CTGTATTCTCCTCAGAAGTT	90	S	1417
1573382	11784	11803	N/A	N/A	TCCCTGTCTTCCACCATCTC	104	S	1418
1573388	14734	14753	N/A	N/A	TGCAGTGGTACCTCCCCTCC	100	S	1419
1573398	5334	5353	N/A	N/A	TCCTGGAGGCTTCATGCCCC	112	S	1420
1573401	12287	12306	712	731	AGGAGGAAAGAGTGAGGTG	93	S	1421
1573419	6547	6566	N/A	N/A	GCCCTCTGTCCTGGGCCACC	109	S	1422
1573425	9092	9111	N/A	N/A	TCTATCAGCAGGTATCTATC	63	S	1423
1573428	5741	5760	N/A	N/A	CTCAATTCTCCATTTCCATC	68	S	1424
1573445	6350	6369	N/A	N/A	ACATAATAAGGGAGGTAGAG	109	S	1425

1573453	7841	7860	N/A	N/A	AACAACACCCACCATAGCAA	92	S	1426
1573488	6394	6413	N/A	N/A	GAAAGAAAGTGCAAAGAAGC	115	S	1427
1573494	6489	6508	N/A	N/A	AAGGTCAGGGAAGAAGGCCA	105	S	1428
1573495	12064	12083	N/A	N/A	TGTAGAAAAGGGAAGACTCA	107	S	1429
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	26	S	70
1573650	5082	5101	N/A	N/A	GCCCCCGGCCCTCAGGCCAG	111	S	1430
1573694	6719	6738	N/A	N/A	ACCTTCAGAGAGGCCCTCAGA	99	S	1431
1573703	11830	11849	N/A	N/A	AGGATCCATCTCAAGCACCT	112	S	1432
1573707	13333	13352	1758	1777	GGAAATGCTCCAGGAGGAGG	95	S	1433
1573721	7889	7908	N/A	N/A	AGACTGGTTTTTAAAATACTA	50	S	1434
1573758	12035	12054	N/A	N/A	TTTTCTTTCTGCTTCCCT	106	S	1435
1574656	18673	18692	4158	4177	GGCACACGATGCTACGCAA	50	S	1436
1572341	6969	6988	N/A	N/A	GAAAAAGAGCCCCCTAAGTAA	100	T	1437
1572374	13790	13809	2215	2234	CCCCGTTTCGGAAGGAGGGAG	110	T	1438
1572382	6863	6882	N/A	N/A	TAAATTTTCAGGATCATTGGC	72	T	1439
1572385	6717	6736	N/A	N/A	CTTCAGAGAGGCCTCAGAGA	106	T	1440
1572390	5034	5053	N/A	N/A	GGGAAAATAACAAATGGAGG	50	T	1441
1572398	5164	5183	N/A	N/A	GGAGACCCTCCCTCCTTCCC	103	T	1442
1572416	12105	12124	530	549	TATCCAGATCGGAGGGAGAC	91†	T	1443
1572420	7475	7494	N/A	N/A	GACCTGGGTCATGTTTTAGC	76	T	1444
1572425	5101	5120	N/A	N/A	GGCGGGCCCCACCCCCTGAG	101	T	1445
1572434	6654	6673	N/A	N/A	CTCAAAGAGAAGTGACTTGC	101	T	1446
1572441	13332	13351	1757	1776	GAAATGCTCCAGGAGGAGGG	85	T	1447
1572471	11911	11930	N/A	N/A	ATTTCTCACTTTTCTCACAT	98	T	1448
1572472	17573	17592	N/A	N/A	TGGAGCTGCCTACCCCAACT	99	T	1449
1572499	12063	12082	N/A	N/A	GTAGAAAAGGGAAGACTCAT	86	T	1450
1572517	12469	12488	894	913	AAAACCTCCACCAGTGCCCCC	80	T	1451
1572520	7888	7907	N/A	N/A	GACTGGTTTTTAAAATACTAT	42	T	1452
1572524	11760	11779	N/A	N/A	CCACCACTTTAACCATCCTC	117	T	1453
1572530	11951	11970	N/A	N/A	GTGAGTACTCTTGCTCAAGC	97	T	1454
1572545	6393	6412	N/A	N/A	AAAGAAAGTGCAAAGAAGCA	118	T	1455
1572549	7567	7586	N/A	N/A	AGGAGAAAAGCAGTCATAAA	94	T	1456
1572603	8948	8967	N/A	N/A	GTTTTCTTCCTTTCCACTGA	39	T	1457
1572630	6488	6507	N/A	N/A	AGGTCAGGGAAGAAGGCCAA	111	T	1458
1572654	11829	11848	N/A	N/A	GGATCCATCTCAAGCACCTT	110	T	1459
1572687	11783	11802	N/A	N/A	CCCTGTCTTCCACCATCTCA	90	T	1460
1572702	13658	13677	2083	2102	CGAGGAAGCCACGGTGCCAA	78	T	1461
1572709	13157	13176	1582	1601	GGCATTGCTGTTGGCTAAGA	17	T	1462
1572773	10458	10477	149	168	CTCCACCCCAAGTTCCCCAC	73	T	1463
1572815	7453	7472	N/A	N/A	CAGCCTACACTCCTAGCAGG	91	T	1464
1572851	12976	12995	1401	1420	GAGGCAGAGGAAGAGGAGGA	67	T	1465
1572888	14730	14749	N/A	N/A	GTGGTACCTCCCCTCCGACA	105	T	1466
1572910	6806	6825	N/A	N/A	AAACCAGTCCAAAGTGACTC	101	T	1467
1572939	6947	6966	N/A	N/A	ACAGGAAAAGAAATTAAGAG	108	T	1468
1572946	12034	12053	N/A	N/A	TTTCCTTTCTGCTTCCCTG	103	T	1469

1572948	6417	6436	N/A	N/A	GAGGAATTCAAGTTTATAGAA	95	T	1470
1572983	14185	14204	N/A	N/A	AAAACACTACACCAGCGCAA	55	T	1471
1572989	5740	5759	N/A	N/A	TCAATTCTCCATTTCCATCC	91	T	1472
1573013	13612	13631	2037	2056	GTGGTGACCGTAGGCACCGG	79	T	1473
1573028	18514	18533	3999	4018	TCCCCATCCTCGCCACCTCC	109	T	1474
1573047	7019	7038	N/A	N/A	AAAAAGAAAATGATTAAGAC	111	T	1475
1573050	13976	13995	2401	2420	CGGCTCCTGTTTGATCTGCG	56	T	1476
1573064	9478	9497	N/A	N/A	GTATTCTCCTCAGAAGTTGC	78	T	1477
1573085	13512	13531	1937	1956	AGGAAGAGTTGGAAGAGGAA	69	T	1478
1573091	7828	7847	N/A	N/A	ATAGCAAAAGAGGAAAACAA	104	T	1479
1573132	14063	14082	2488	2507	ATGGCTGGGTACATCTACCA	68	T	1480
1573157	7914	7933	N/A	N/A	TTCCCACATTTTTTAGTTGT	85	T	1481
1573162	6373	6392	N/A	N/A	AAAAGACAACCTCTACAAAAA	117	T	1482
1573167	5081	5100	N/A	N/A	CCCCCGGCCCTCAGGCCAGG	111	T	1483
1573177	7522	7541	N/A	N/A	AGTGGCAGACGAGGAAAGGA	75	T	1484
1573197	16038	16057	N/A	N/A	AAAAAAATAAATAAGAAGAC	102	T	1485
1573206	7407	7426	N/A	N/A	CACCTACTCTGTATCTGGCC	46	T	1486
1573208	12170	12189	595	614	GTTGTCCTGGTCGATATCCC	22†	T	1487
1573307	6287	6306	N/A	N/A	GTTTTCATCCTCCCATCATG	60	T	1488
1573370	6546	6565	N/A	N/A	CCCTCTGTCCTGGGCCACCC	64	T	1489
1573404	5332	5351	N/A	N/A	CTGGAGGCTTCATGCCCCAC	86	T	1490
1573407	18175	18194	N/A	N/A	GGGTTCCTCCCCAGGAGC	112	T	1491
1573417	7761	7780	N/A	N/A	TTTTGCCAGCCCTCCTAGAG	84	T	1492
1573497	7633	7652	N/A	N/A	ATCATAGTATGCCCTTCTTT	45	T	1493
1573508	7609	7628	N/A	N/A	ATCACCTGAAATCTGATAAA	103	T	1494
1573549	11885	11904	N/A	N/A	CTGCTCCCTAGCAGCCAGTC	95	T	1495
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	23	T	70
1573587	6754	6773	N/A	N/A	ACGATGCACTGGCCTAAGCC	89	T	1496
1573602	6448	6467	N/A	N/A	GAAAAGGGTTACTCAAGAAG	76	T	1497
1573603	15195	15214	2924	2943	AGAATGGATGGTTGCGATTG	45	T	1498
1573613	12375	12394	800	819	GAGCATGATATCCAGTGGGT	20	T	1499
1573626	14084	14103	N/A	N/A	TCACCTGGCAGACTGACTGG	92	T	1500
1573640	7655	7674	N/A	N/A	AATGTACCTGAGGAACACAG	78	T	1501
1573645	8779	8798	N/A	N/A	ATGTCCATATTCTGTAGTGT	9	T	1502
1573652	12827	12846	1252	1271	CTCTGGGCCAGGAGGAAGTC	98	T	1503
1573684	11104	11123	N/A	N/A	TTCCCACCTCAGTTTTGGTC	78†	T	1504
1573689	6343	6362	N/A	N/A	AAGGGAGGTAGAGGTCAGAA	82	T	1505
1573690	14277	14296	N/A	N/A	GCCCCGCCTCAAAACCACC	109	T	1506
1573708	12547	12566	972	991	GGGTGCTGCTTACCCCCATT	93	T	1507
1573740	7703	7722	N/A	N/A	CACCAAGTCAGTTAGGTTAG	44	T	1508
1573755	12286	12305	711	730	GGAGGAAAGAGTGGAGGTGG	87	T	1509
1573796	7802	7821	N/A	N/A	ACAAAAAGCACAAACAAGAT	108	T	1510
1573814	9091	9110	N/A	N/A	CTATCAGCAGGTATCTATCT	69	T	1511
1573852	18648	18667	4133	4152	CACATCTAACAGATGAAATA	110	T	1512
1573864	7736	7755	N/A	N/A	TGTCCATCTCCCTTCCCAT	49	T	1513

1572339	11948	11967	N/A	N/A	AGTACTCTTGCTCAAGCCCA	82	U	1514
1572384	7566	7585	N/A	N/A	GGAGAAAAGCAGTCATAAAA	93	U	1515
1572419	7452	7471	N/A	N/A	AGCCTACACTCCTAGCAGGC	67	U	1516
1572459	12544	12563	969	988	TGCTGCTTACCCCCATTAGG	29	U	1517
1572461	6653	6672	N/A	N/A	TCAAAGAGAAGTGACTTGCC	85	U	1518
1572462	12975	12994	1400	1419	AGGCAGAGGAAGAGGAGGAA	65	U	1519
1572464	7913	7932	N/A	N/A	TCCCACATTTTTTTAGTTGTT	19	U	1520
1572465	18513	18532	3998	4017	CCCCATCCTCGCCACCTCCC	90	U	1521
1572477	11884	11903	N/A	N/A	TGCTCCCTAGCAGCCAGTCT	88	U	1522
1572491	9089	9108	N/A	N/A	ATCAGCAGGTATCTATCTTT	58	U	1523
1572498	8768	8787	N/A	N/A	CTGTAGTGTATTTTTTCCCA	21	U	1524
1572516	11782	11801	N/A	N/A	CCTGTCCTCCACCATCTCAT	125	U	1525
1572535	7701	7720	N/A	N/A	CCAAGTCAGTTAGGTTAGGG	8	U	1526
1572540	6716	6735	N/A	N/A	TTCAGAGAGGCCTCAGAGAT	74	U	1527
1572551	12468	12487	893	912	AAACTCCACCAGTGCCCCCA	46	U	1528
1572648	5331	5350	N/A	N/A	TGGAGGCTTCATGCCCCACC	93	U	1529
1572667	5080	5099	N/A	N/A	CCCCGGCCCTCAGGCCAGGC	90	U	1530
1572690	14698	14717	N/A	N/A	ACTCGCCCGCCACCCAGCC	79	U	1531
1572705	7632	7651	N/A	N/A	TCATAGTATGCCCTTCTTTT	36	U	1532
1572766	16037	16056	N/A	N/A	AAAAAATAAATAAGAAGACA	88	U	1533
1572849	7608	7627	N/A	N/A	TCACCTGAAATCTGATAAAA	81	U	1534
1572880	12062	12081	N/A	N/A	TAGAAAAGGGAAGACTCATT	66	U	1535
1572914	7826	7845	N/A	N/A	AGCAAAAGAGGAAAACAATC	111	U	1536
1572988	15194	15213	2923	2942	GAATGGATGGTTGCGATTGC	24	U	1537
1573018	18173	18192	N/A	N/A	GTTCCCTCCCCCAGGAGCAC	75	U	1538
1573030	5739	5758	N/A	N/A	CAATTCTCCATTTCCATCCT	81	U	1539
1573061	7520	7539	N/A	N/A	TGGCAGACGAGGAAAGGAGT	63	U	1540
1573118	6487	6506	N/A	N/A	GGTCAGGGAAGAAGGCCAAA	72	U	1541
1573139	7759	7778	N/A	N/A	TTGCCAGCCCTCCTAGAGAA	92	U	1542
1573160	6846	6865	N/A	N/A	GGCCCAGCCCCAACATCAT	78	U	1543
1573168	6753	6772	N/A	N/A	CGATGCACTGGCCTAAGCCT	65	U	1544
1573203	17561	17580	N/A	N/A	CCCCAACTTCCATCCTTACC	112	U	1545
1573242	5033	5052	N/A	N/A	GGAAAATAACAAATGGAGGC	44	U	1546
1573243	12169	12188	594	613	TTGTCTGGTTCGATATCCCT	28†	U	1547
1573244	14276	14295	N/A	N/A	CCCCCGCCTCAAACCACCC	69	U	1548
1573248	12285	12304	710	729	GAGGAAAGAGTGGAGGTGGG	81	U	1549
1573266	13611	13630	2036	2055	TGGTGACCGTAGGCACCGGT	92	U	1550
1573310	13926	13945	2351	2370	CCGCAGGTGGTGGTGGCAGC	75	U	1551
1573366	6372	6391	N/A	N/A	AAAGACAACCTCTACAAAAAA	125	U	1552
1573378	14061	14080	2486	2505	GGCTGGGTACATCTACCACC	50	U	1553
1573383	12374	12393	799	818	AGCATGATATCCAGTGGGTG	12	U	332
1573406	12826	12845	1251	1270	TCTGGGCCAGGAGGAAGTCC	114	U	1554
1573446	12033	12052	N/A	N/A	TTCCTTTCCTGCTTCCCTGA	65	U	1555
1573451	10212	10231	N/A	N/A	CCCCATGGGCTACCTTAGCT	120	U	1556
1573460	7406	7425	N/A	N/A	ACCTACTCTGTATCTGGCCA	54	U	1557

1573464	13510	13529	1935	1954	GAAGAGTTGGAAGAGGAAGA	59	U	1558
1573472	9456	9475	N/A	N/A	GGGAGAATTCTCAGAAGGCC	60	U	1559
1573473	6416	6435	N/A	N/A	AGGAATTCAAGTTTTAGAAA	72	U	1560
1573490	5163	5182	N/A	N/A	GAGACCCTCCCTCCTTCCCC	75	U	1561
1573493	11828	11847	N/A	N/A	GATCCATCTCAAGCACCTTG	67	U	1562
1573515	18644	18663	4129	4148	TCTAACAGATGAAATAATCA	73	U	1563
1573525	11103	11122	N/A	N/A	TCCCACCTCAGTTTTGGTCT	69†	U	1564
1573532	13156	13175	1581	1600	GCATTGCTGTTGGCTAAGAG	20	U	1565
1573534	12104	12123	529	548	ATCCAGATCGGAGGGAGACT	63†	U	1566
1573537	13311	13330	1736	1755	GCCCAGAGTTTCCGTGATGC	27	U	1567
1573544	8883	8902	N/A	N/A	CAGTAGGTCTTTCTTCCTGA	43	U	1568
1573556	7801	7820	N/A	N/A	CAAAAAGCACAAACAAAGATG	81	U	1569
1573559	6286	6305	N/A	N/A	TTTTCATCCTCCCATCATGC	88	U	1570
1573560	6392	6411	N/A	N/A	AAGAAAGTGCAAAGAAGCAA	83	U	1571
1573564	6915	6934	N/A	N/A	TGTCAGAAGGAATACAGTGG	62	U	1572
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	18	U	70
1573588	7018	7037	N/A	N/A	AAAAGAAAATGATTAAGACC	99	U	1573
1573630	6805	6824	N/A	N/A	AACCAGTCCAAAGTGACTCC	68	U	1574
1573719	6342	6361	N/A	N/A	AGGGAGGTAGAGGTCAGAAC	63	U	1575
1573733	7474	7493	N/A	N/A	ACCTGGGTCATGTTTATAGCA	48	U	1576
1573749	6447	6466	N/A	N/A	AAAAGGGTTACTCAAGAAGG	84	U	1577
1573774	6968	6987	N/A	N/A	AAAAAGAGCCCCCTAAGTAAG	78	U	1578
1573802	13789	13808	2214	2233	CCCGTTCGGAAGGAGGGAGG	68	U	1579
1573806	7654	7673	N/A	N/A	ATGTACCTGAGGAACACAGC	77	U	1580
1573813	14164	14183	N/A	N/A	GCCCCTCCCTGCTACTCCCT	66	U	1581
1573832	13657	13676	2082	2101	GAGGAAGCCACGGTGGCAAT	57	U	1582
1573843	6545	6564	N/A	N/A	CCTCTGTCCTGGGCCACCCT	82	U	1583
1573848	14083	14102	N/A	N/A	CACCTGGCAGACTGACTGGC	75	U	1584
1573849	7735	7754	N/A	N/A	GTCCATCTCCCTTCCCCATC	31	U	1585
1573851	11750	11769	N/A	N/A	AACCATCCTCCATCCCCCAA	70	U	1586
1573853	7887	7906	N/A	N/A	ACTGGTTTTTAAATACTATC	34	U	1587
1573862	11909	11928	N/A	N/A	TTCTCACTTTCCTCACATTC	107	U	1588
1573865	5100	5119	N/A	N/A	GCGGGCCCCACCCCTGAGC	79	U	1589
1475594	9088	9107	N/A	N/A	TCAGCAGGTATCTATCTTTA	16	V	590
1572347	5032	5051	N/A	N/A	GAAAATAACAAATGGAGGCG	73	V	1590
1572350	11947	11966	N/A	N/A	GTACTCTTGCTCAAGCCCAC	64	V	1591
1572356	13155	13174	1580	1599	CATTGCTGTTGGCTAAGAGG	16	V	1592
1572364	13788	13807	2213	2232	CCGTTCGGAAGGAGGGAGGC	63	V	1593
1572366	12530	12549	955	974	ATTAGGGCCCCCACTGATG	65	V	1594
1572367	7674	7693	N/A	N/A	AAGGTCAGAGAAACACAGGA	41	V	1595
1572426	11827	11846	N/A	N/A	ATCCATCTCAAGCACCTTGT	62	V	1596
1572427	6752	6771	N/A	N/A	GATGCACTGGCCTAAGCCTT	62	V	1597
1572435	6484	6503	N/A	N/A	CAGGGAAGAAGGCCAAAGGT	70	V	1598
1572436	12103	12122	528	547	TCCAGATCGGAGGGAGACTG	62†	V	1599
1572447	7653	7672	N/A	N/A	TGTACCTGAGGAACACAGCA	48	V	1600

1572455	9455	9474	N/A	N/A	GGAGAATTCTCAGAAGGCCT	91	V	1601
1572469	5150	5169	N/A	N/A	CTTCCCCACCTTCCCGATCC	70	V	1602
1572489	11074	11093	467	486	CATTGGTCTCCTCACTTTCA	30†	V	1603
1572538	6285	6304	N/A	N/A	TTTCATCCTCCCATCATGCC	84	V	1604
1572554	9684	9703	N/A	N/A	CCTTCACATACATGATTTCA	58	V	1605
1572563	7607	7626	N/A	N/A	CACCTGAAATCTGATAAAAA	88	V	1606
1572591	12467	12486	892	911	AACTCCACCAGTGCCCCCAG	41	V	1607
1572633	13656	13675	2081	2100	AGGAAGCCACGGTGGCAATG	61	V	1608
1572649	14058	14077	2483	2502	TGGGTACATCTACCACCTTG	84	V	1609
1572658	13919	13938	2344	2363	TGGTGGTGGCAGCGATGGCA	29	V	1610
1572677	7912	7931	N/A	N/A	CCCACATTTTTTAGTTGTTA	21	V	1611
1572701	18512	18531	3997	4016	CCCATCCTCGCCACCTCCCC	64	V	1612
1572768	12371	12390	796	815	ATGATATCCAGTGGGTGTCA	36	V	1613
1572789	15193	15212	2922	2941	AATGGATGGTTGCGATTGCC	16	V	196
1572835	12032	12051	N/A	N/A	TCCTTTCCTGCTTCCCTGAG	96	V	1614
1572869	7451	7470	N/A	N/A	GCCTACACTCCTAGCAGGCA	72	V	1615
1572912	18110	18129	N/A	N/A	GAGCCCATGTCCCCTGGGCT	68	V	1616
1572913	14696	14715	N/A	N/A	TCGCCCCGCCACCCAGCCAC	72	V	1617
1572949	7473	7492	N/A	N/A	CCTGGGTCATGTTTTAGCAC	72	V	1618
1572956	5099	5118	N/A	N/A	CGGGCCCCACCCCCTGAGCC	73	V	1619
1572958	11749	11768	N/A	N/A	ACCATCCTCCATCCCCCAAG	122	V	1620
1572968	14275	14294	N/A	N/A	CCCCGCCTCAAAACCACCCC	132	V	1621
1572972	13310	13329	1735	1754	CCCAGAGTTTCCGTGATGCT	14	V	1622
1572976	15976	15995	N/A	N/A	AAAGTGTCCTTCAAAAGCTC	128	V	1623
1573003	6341	6360	N/A	N/A	GGGAGGTAGAGGTCAGAACC	101	V	1624
1573006	5330	5349	N/A	N/A	GGAGGCTTCATGCCCCACCT	112	V	1625
1573038	7405	7424	N/A	N/A	CCTACTCTGTATCTGGCCAC	50	V	1626
1573039	13496	13515	1921	1940	GGAAGAGACTGGAGGGCCAT	53	V	1627
1573044	17353	17372	N/A	N/A	GGCAAACCATGCATTTGGGT	63	V	1628
1573058	6370	6389	N/A	N/A	AGACAACTCTACAAAAAATA	92	V	1629
1573082	6715	6734	N/A	N/A	TCAGAGAGGCCTCAGAGATC	86	V	1630
1573110	12284	12303	709	728	AGGAAAGAGTGGAGGTGGGT	76	V	1631
1573116	7886	7905	N/A	N/A	CTGGTTTTAAATACTATCA	26	V	1632
1573181	11883	11902	N/A	N/A	GCTCCCTAGCAGCCAGTCTT	68	V	1633
1573228	6391	6410	N/A	N/A	AGAAAGTGCAAAGAAGCAAA	123	V	1634
1573235	8764	8783	N/A	N/A	AGTGTATTTTTTCCCAAGAA	12	V	1635
1573268	5737	5756	N/A	N/A	ATTCTCCATTTCCATCCTCC	56	V	1636
1573271	14082	14101	2507	2526	ACCTGGCAGACTGACTGGCA	53	V	1637
1573314	12973	12992	1398	1417	GCAGAGGAAGAGGAGGAAGA	56	V	1638
1573326	6544	6563	N/A	N/A	CTCTGTCCTGGGCCACCCTC	71	V	1639
1573375	7825	7844	N/A	N/A	GCAAAAGAGGAAAACAATCT	61	V	1640
1573391	12825	12844	1250	1269	CTGGGCCAGGAGGAAGTCCA	69	V	1641
1573396	6613	6632	N/A	N/A	CAGGTCTAGACACAGGTCTC	58	V	1642
1573405	11780	11799	N/A	N/A	TGTCTTCCACCATCTCATAA	76	V	1643
1573463	7757	7776	N/A	N/A	GCCAGCCCTCCTAGAGAAGG	60	V	1644

1573475	8882	8901	N/A	N/A	AGTAGGTCTTTCTTCCTGAA	37	V	1645
1573484	7799	7818	N/A	N/A	AAAAGCACAACAAAGATGAC	72	V	1646
1573485	7734	7753	N/A	N/A	TCCATCTCCCTTCCCCATCA	54	V	1647
1573578	7564	7583	N/A	N/A	AGAAAAGCAGTCATAAAAGA	65	V	1648
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	21	V	70
1573614	7017	7036	N/A	N/A	AAAGAAAATGATTAAGACCA	71	V	1649
1573646	12061	12080	N/A	N/A	AGAAAAGGGAAGACTCATTT	89	V	1650
1573660	11908	11927	N/A	N/A	TCTCACTTTCCTCACATTCT	101	V	1651
1573663	6804	6823	N/A	N/A	ACCAGTCCAAAGTGACTCCT	104	V	1652
1573675	13610	13629	2035	2054	GGTGACCGTAGGCACCGGTG	70	V	1653
1573676	14162	14181	N/A	N/A	CCCTCCCTGCTACTCCCTCT	72	V	1654
1573701	6442	6461	N/A	N/A	GGTTACTCAAGAAGGGAGGC	69	V	1655
1573738	7519	7538	N/A	N/A	GGCAGACGAGGAAAGGAGTT	43	V	1656
1573743	6914	6933	N/A	N/A	GTCAGAAAGGAATACAGTGGA	45	V	1657
1573747	6835	6854	N/A	N/A	CAACATCATTCTGGACCTGC	46	V	1658
1573748	7631	7650	N/A	N/A	CATAGTATGCCCTTCTTTTT	38	V	1659
1573763	12168	12187	593	612	TGTCCTGGTCGATATCCCTA	21†	V	1660
1573777	5079	5098	N/A	N/A	CCCGGCCCTCAGGCCAGGCA	72	V	1661
1573799	6967	6986	N/A	N/A	AAAAGAGCCCCTAAGTAAGA	72	V	1662
1573819	6415	6434	N/A	N/A	GGAATTCAAGTTTTAGAAAA	76	V	1663
1574653	18558	18577	4043	4062	GGACAAGGAAGAGAGACCTG	72	V	1664
1475507	9087	9106	N/A	N/A	CAGCAGGTATCTATCTTTAT	10	W	643
1572334	7652	7671	N/A	N/A	GTACCTGAGGAACACAGCAA	69	W	1665
1572340	7472	7491	N/A	N/A	CTGGGTCATGTTTTAGCACC	26	W	1666
1572354	7733	7752	N/A	N/A	CCATCTCCCTTCCCCATCAC	75	W	1667
1572357	11946	11965	N/A	N/A	TACTCTTGCTCAAGCCCACC	99	W	1668
1572365	6543	6562	N/A	N/A	TCTGTCCTGGGCCACCCTCA	89	W	1669
1572389	7798	7817	N/A	N/A	AAAGCACAACAAAGATGACT	84	W	1670
1572404	18554	18573	4039	4058	AAGGAAGAGAGACCTGGTCC	63	W	1671
1572410	7756	7775	N/A	N/A	CCAGCCCTCCTAGAGAAGGG	63	W	1672
1572411	6441	6460	N/A	N/A	GTTACTCAAGAAGGGAGGCT	82	W	1673
1572412	6803	6822	N/A	N/A	CCAGTCCAAAGTGACTCCTA	70	W	1674
1572422	18511	18530	3996	4015	CCATCCTCGCCACCTCCCCA	84	W	1675
1572502	11826	11845	N/A	N/A	TCCATCTCAAGCACCTTGTC	88	W	1676
1572526	11907	11926	N/A	N/A	CTCACTTTCCTCACATTCTT	106	W	1677
1572567	12283	12302	708	727	GGAAAGAGTGAGGTGGGTG	93	W	1678
1572595	7885	7904	N/A	N/A	TGGTTTTAAAATACTATCAA	71	W	1679
1572621	7016	7035	N/A	N/A	AAGAAAATGATTAAGACCAG	77	W	1680
1572631	6390	6409	N/A	N/A	GAAAGTGCAAAGAAGCAAAA	88	W	1681
1572681	15192	15211	2921	2940	ATGGATGGTTGCGATTGCCA	16	W	1682
1572725	15975	15994	N/A	N/A	AAGTGTCTTCAAAAAGCTCC	84	W	1683
1572737	12939	12958	1364	1383	CTGCTGCAGAGCTACTACTA	51	W	1684
1572754	7563	7582	N/A	N/A	GAAAAGCAGTCATAAAAGAA	90	W	1685
1572779	5078	5097	N/A	N/A	CCGGCCCTCAGGCCAGGCAG	91	W	1686
1572790	14695	14714	N/A	N/A	CGCCCGCCACCCAGCCACA	95	W	1687

1572806	9413	9432	N/A	N/A	AAGAATCTTTTCTCACATCA	55	W	1688
1572811	11072	11091	465	484	TTGGTCTCCTCACTTTTCACT	9†	W	1689
1572845	12031	12050	N/A	N/A	CCTTTCCTGCTTCCCTGAGA	93	W	1690
1572853	6369	6388	N/A	N/A	GACAACTCTACAAAAAATAA	86	W	1691
1572860	7435	7454	N/A	N/A	GGCAATCACTGTAACATAA	20	W	1692
1572896	7630	7649	N/A	N/A	ATAGTATGCCCTTCTTTTTT	44	W	1693
1572915	11881	11900	N/A	N/A	TCCCTAGCAGCCAGTCTTGT	97	W	1694
1572923	13309	13328	1734	1753	CCAGAGTTTCCGTGATGCTG	14	W	1695
1572929	12369	12388	794	813	GATATCCAGTGGGTGTCACA	30	W	1696
1572936	6834	6853	N/A	N/A	AACATCATTCTGGACCTGCC	58	W	1697
1572961	17872	17891	N/A	N/A	GGGCATATGACCAACGGATA	79	W	1698
1572962	6913	6932	N/A	N/A	TCAGAAGGAATACAGTGGAG	85	W	1699
1572985	6751	6770	N/A	N/A	ATGCACTGGCCTAAGCCTTC	95	W	1700
1573026	8881	8900	N/A	N/A	GTAGGTCTTTCTTCTGAAT	52	W	1701
1573034	17313	17332	N/A	N/A	ACTGAGTCAGACAAACACAA	100	W	1702
1573077	13154	13173	1579	1598	ATTGCTGTTGGCTAAGAGGC	19	W	1703
1573080	12102	12121	527	546	CCAGATCGGAGGGAGACTGT	80†	W	1704
1573087	12060	12079	N/A	N/A	GAAAAGGGAAGACTCATTTT	86	W	1705
1573103	14161	14180	N/A	N/A	CCTCCCTGCTACTCCCTCTC	83	W	1706
1573107	14080	14099	2505	2524	CTGGCAGACTGACTGGCATG	59	W	1707
1573138	6966	6985	N/A	N/A	AAAGAGCCCCTAAGTAAGAA	93	W	1708
1573190	12529	12548	954	973	TTAGGGCCCCCCTGATGA	95	W	1709
1573210	13655	13674	2080	2099	GGAAGCCACGGTGGCAATGA	65	W	1710
1573213	8763	8782	N/A	N/A	GTGTATTTTTTCCCAAGAAA	16	W	1711
1573220	7606	7625	N/A	N/A	ACCTGAAATCTGATAAAAAC	95	W	1712
1573230	11748	11767	N/A	N/A	CCATCCTCCATCCCCAAGC	102	W	1713
1573253	12167	12186	592	611	GTCCTGGTGCATATCCCTAG	26†	W	1714
1573305	6414	6433	N/A	N/A	GAATCAAGTTTATAGAAAAT	95	W	1715
1573306	13470	13489	1895	1914	CTGCTTGGCTGTAGGACACC	17	W	1716
1573340	11779	11798	N/A	N/A	GTCTTCCACCATCTCATAAC	82	W	1717
1573342	6714	6733	N/A	N/A	CAGAGAGGCCTCAGAGATCA	71	W	1718
1573351	7389	7408	N/A	N/A	CCACATACTAAGCACATTCA	58	W	1719
1573365	7518	7537	N/A	N/A	GCAGACGAGGAAAGGAGTTA	87	W	1720
1573369	13787	13806	2212	2231	CGTTCGGAAGGAGGGAGGCG	83	W	1721
1573442	12466	12485	891	910	ACTCCACCAGTGCCCCCAGG	34	W	1722
1573467	5031	5050	N/A	N/A	AAAATAACAAATGGAGGCGG	61	W	1723
1573476	6612	6631	N/A	N/A	AGGTCTAGACACAGGTCTCC	81	W	1724
1573491	5098	5117	N/A	N/A	GGGCCCCACCCCTGAGCCC	95	W	1725
1573496	5316	5335	N/A	N/A	CCACCTCGCTGCCATCTCTC	86	W	1726
1573550	14056	14075	2481	2500	GGTACATCTACCACCTTGGG	46	W	1727
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	24	W	70
1573583	13918	13937	2343	2362	GGTGGTGGCAGCGATGGCAG	45	W	1728
1573644	6284	6303	N/A	N/A	TTCATCCTCCCATCATGCCC	82	W	1729
1573669	7911	7930	N/A	N/A	CCACATTTTTTAGTTGTTAT	15	W	1730
1573673	5146	5165	N/A	N/A	CCCACCTTCCCGATCCTCCC	91	W	1731

1573679	7673	7692	N/A	N/A	AGGTCAGAGAAACACAGGAA	40	W	1732
1573681	13608	13627	2033	2052	TGACCGTAGGCACCGGTGGG	79	W	1733
1573686	5685	5704	N/A	N/A	TGTTCTGTTTTCTCTCTCA	52	W	1734
1573752	6483	6502	N/A	N/A	AGGGAAGAAGGCCAAAGGTT	79	W	1735
1573779	6339	6358	N/A	N/A	GAGGTAGAGGTCAGAACCAA	79	W	1736
1573784	12823	12842	1248	1267	GGGCCAGGAGGAAGTCCACC	75	W	1737
1573794	7824	7843	N/A	N/A	CAAAAGAGGAAAACAATCTT	104	W	1738
1573804	9683	9702	N/A	N/A	CTTCACATACATGATTTCAT	46	W	1739
1573809	14274	14293	N/A	N/A	CCCGCCTCAAACCACCCCT	105	W	1740
1572332	5030	5049	N/A	N/A	AAATAACAAATGGAGGCGGC	67	X	1741
1572443	14054	14073	2479	2498	TACATCTACCACCTTGGGAG	26	X	1742
1572453	13467	13486	1892	1911	CTTGCTGTAGGACACCTGG	35	X	1743
1572481	5097	5116	N/A	N/A	GGCCCCACCCCCTGAGCCCC	90	X	1744
1572497	12822	12841	1247	1266	GGCCAGGAGGAAGTCCACCC	64	X	1745
1572508	12936	12955	1361	1380	CTGCAGAGCTACTACTAGAG	42	X	1746
1572556	7629	7648	N/A	N/A	TAGTATGCCCTTCTTTTTTA	45	X	1747
1572561	7562	7581	N/A	N/A	AAAAGCAGTCATAAAAGAAC	79	X	1748
1572573	14272	14291	N/A	N/A	CGCCTCAAACCACCCCTGC	103	X	1749
1572589	5491	5510	N/A	N/A	GACCTCTCTTTGCCCAAGCC	74	X	1750
1572618	6541	6560	N/A	N/A	TGTCCTGGGCCACCCCTACC	96	X	1751
1572625	7909	7928	N/A	N/A	ACATTTTTTAGTTGTTATGT	62	X	1752
1572642	14160	14179	N/A	N/A	CTCCCTGCTACTCCCTCTCT	99	X	1753
1572644	11071	11090	464	483	TGGTCTCCTCACTTCACTC	8 ⁺	X	1754
1572647	13654	13673	2079	2098	GAAGCCACGGTGGCAATGAC	80	X	1755
1572655	11945	11964	N/A	N/A	ACTCTTGCTCAAGCCCACCT	74	X	1756
1572660	7755	7774	N/A	N/A	CAGCCCTCCTAGAGAAGGGT	95	X	1757
1572668	6965	6984	N/A	N/A	AAGAGCCCCTAAGTAAGAAC	95	X	1758
1572727	6337	6356	N/A	N/A	GGTAGAGGTCAGAACCAACT	64	X	1759
1572740	6482	6501	N/A	N/A	GGGAAGAAGGCCAAAGGTTA	88	X	1760
1572743	6283	6302	N/A	N/A	TCATCCTCCCATCATGCCCA	69	X	1761
1572751	11778	11797	N/A	N/A	TCTTCCACCATCTCATAACC	86	X	1762
1572757	11880	11899	N/A	N/A	CCCTAGCAGCCAGTCTTGTT	84	X	1763
1572771	9681	9700	N/A	N/A	TCACATACATGATTTCATTT	44	X	1764
1572776	9265	9284	N/A	N/A	TCTAGTACTTGAGCTCCCTA	61	X	1765
1572784	7884	7903	N/A	N/A	GGTTTAAATACTATCAAC	53	X	1766
1572787	7434	7453	N/A	N/A	GCAATCACTGTAACATAATAT	46	X	1767
1572822	7015	7034	N/A	N/A	AGAAAATGATTAAGACCAGA	80	X	1768
1572834	6912	6931	N/A	N/A	CAGAAGGAATACAGTGGAGT	68	X	1769
1572887	17871	17890	N/A	N/A	GGCATATGACCAACGGATAA	85	X	1770
1572903	7672	7691	N/A	N/A	GGTCAGAGAAACACAGGAAT	32	X	1771
1572904	12030	12049	N/A	N/A	CTTTCCTGCTTCCCTGAGAT	81	X	1772
1572951	6413	6432	N/A	N/A	AATTCAAGTTTTAGAAAATG	73	X	1773
1572954	11825	11844	N/A	N/A	CCATCTCAAGCACCTTGTCT	84	X	1774
1572969	7797	7816	N/A	N/A	AAGCACAACAAAGATGACTA	63	X	1775
1572996	6749	6768	N/A	N/A	GCACTGGCCTAAGCCTTCTG	76	X	1776

1573010	8879	8898	N/A	N/A	AGGTCTTTCTTCTGAATTA	43	X	1777
1573054	8746	8765	N/A	N/A	AAACACAGTAATTCTCACTC	70	X	1778
1573111	11906	11925	N/A	N/A	TCACCTTCTCACATTCTTG	75	X	1779
1573158	12364	12383	789	808	CCAGTGGGTGTACAGAAGG	40	X	1780
1573209	12059	12078	N/A	N/A	AAAAGGGAAGACTCATTTTT	107	X	1781
1573229	7495	7514	N/A	N/A	GTGGATTGTGTCTTTCTA	25	X	1782
1573231	7651	7670	N/A	N/A	TACCTGAGGAACACAGCAAT	94	X	1783
1573233	15974	15993	N/A	N/A	AGTGCCTTCAAAAGCTCCC	96	X	1784
1573249	12528	12547	953	972	TAGGGCCCCCCTGATGAG	88	X	1785
1573290	13603	13622	2028	2047	GTAGGCACCGGTGGGAAAGG	92	X	1786
1573303	7605	7624	N/A	N/A	CCTGAAATCTGATAAAACT	85	X	1787
1573349	6713	6732	N/A	N/A	AGAGAGGCCTCAGAGATCAT	94	X	1788
1573353	5302	5321	N/A	N/A	TCTCTCTATCCATTCTGCC	69	X	1789
1573439	5145	5164	N/A	N/A	CCACCTTCCCGATCCTCCCG	101	X	1790
1573462	13308	13327	1733	1752	CAGAGTTTCCGTGATGCTGC	22	X	416
1573498	7471	7490	N/A	N/A	TGGGTCATGTTTTAGACCA	56	X	1791
1573506	17310	17329	N/A	N/A	GAGTCAGACAAACACAAGGA	87	X	1792
1573518	13917	13936	2342	2361	GTGGTGGCAGCGATGGCAGG	56	X	1793
1573519	6785	6804	N/A	N/A	TAGATAACAATGCAGCCCAG	85	X	1794
1573526	12166	12185	591	610	TCCTGGTCGATATCCCTAGG	47†	X	1795
1573569	18510	18529	3995	4014	CATCCTCGCCACCTCCCCAC	91	X	1796
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	23	X	70
1573596	6368	6387	N/A	N/A	ACAACCTCTACAAAAATAAC	92	X	1797
1573604	6389	6408	N/A	N/A	AAAGTGCAAAGAAGCAAAAA	95	X	1798
1573610	7375	7394	N/A	N/A	CATTCACCTTCATTACCTTG	55	X	1799
1573611	6440	6459	N/A	N/A	TTACTCAAGAAGGGAGGCTC	70	X	1800
1573621	9086	9105	N/A	N/A	AGCAGGTATCTATCTTTATC	14	X	1801
1573704	15190	15209	2919	2938	GGATGGTTGCGATTGCCAGG	42	X	1802
1573715	12101	12120	526	545	CAGATCGGAGGGAGACTGTG	73†	X	1803
1573717	7823	7842	N/A	N/A	AAAAGAGGAAAACAATCTTA	84	X	1804
1573722	13150	13169	1575	1594	CTGTTGGCTAAGAGGCGGCC	82	X	1805
1573732	13674	13693	2099	2118	TTTTGTAGCCTGCTGGCGAG	71	X	1806
1573750	12282	12301	707	726	GAAAGAGTGGAGGTGGGTGG	86	X	1807
1573769	14079	14098	2504	2523	TGGCAGACTGACTGGCATGG	55	X	1808
1573771	12465	12484	890	909	CTCCACCACTGCCCCCAGGA	48	X	1809
1573785	7732	7751	N/A	N/A	CATCTCCCTTCCCCATCACA	92	X	1810
1573786	14694	14713	N/A	N/A	GCCCCGCCACCCAGCCACAG	96	X	1811
1573835	11747	11766	N/A	N/A	CATCCTCCATCCCCCAAGCC	94	X	1812
1573841	6833	6852	N/A	N/A	ACATCATTCTGGACCTGCCA	44	X	1813
1573842	6610	6629	N/A	N/A	GTCTAGACACAGGTCTCCTG	97	X	1814
1573847	5077	5096	N/A	N/A	CGGCCCTCAGGCCAGGCAGA	74	X	1815
1574652	18553	18572	4038	4057	AGGAAGAGAGACCTGGTCCA	49	X	1816
1475384	7374	7393	N/A	N/A	ATTCACCTTCATTACCTTGC	23	Y	841
1475398	9085	9104	N/A	N/A	GCAGGTATCTATCTTTATCC	15	Y	694
1572372	7424	7443	N/A	N/A	TAACATAATTACAGAGCAC	79	Y	1817

1572386	6412	6431	N/A	N/A	ATTCAAGTTTTAGAAAATGA	84	Y	1818
1572405	6748	6767	N/A	N/A	CACTGGCCTAAGCCTTCTGA	95	Y	1819
1572406	12821	12840	1246	1265	GCCAGGAGGAAGTCCACCCA	72	Y	1820
1572448	12363	12382	788	807	CAGTGGGTGTACAGAAGGA	20	Y	1821
1572474	5301	5320	N/A	N/A	CTCTCCTATCCATTCTGCCT	82	Y	1822
1572493	8743	8762	N/A	N/A	CACAGTAATTCTCACTCACC	81	Y	1823
1572501	5489	5508	N/A	N/A	CCTCTCTTTGCCCAAGCCTC	76	Y	1824
1572518	12462	12481	887	906	CACCAGTGCCCCCAGGATAG	55	Y	1825
1572536	12029	12048	N/A	N/A	TTTCCTGCTTCCCTGAGATT	88	Y	1826
1572546	8873	8892	N/A	N/A	TTCTTCCTGAATTAAGTGCT	59	Y	1827
1572585	14159	14178	N/A	N/A	TCCCTGCTACTCCCTCTCTC	78	Y	1828
1572586	13916	13935	2341	2360	TGGTGGCAGCGATGGCAGGC	39	Y	1829
1572588	12058	12077	N/A	N/A	AAAGGGAAGACTCATTTTTT	76	Y	1830
1572596	7822	7841	N/A	N/A	AAAGAGGAAAACAATCTTAA	90	Y	1831
1572632	12527	12546	952	971	AGGGCCCCCCTGATGAGG	82	Y	1832
1572641	11905	11924	N/A	N/A	CACCTTCCTCACATTCTTGG	80	Y	1833
1572650	12165	12184	590	609	CCTGGTCGATATCCCTAGGG	61†	Y	1834
1572685	6911	6930	N/A	N/A	AGAAGGAATACAGTGGAGTC	62	Y	1835
1572720	14693	14712	N/A	N/A	CCCGCCACCCAGCCACAGC	84	Y	1836
1572793	11879	11898	N/A	N/A	CCTAGCAGCCAGTCTTGTTT	91	Y	1837
1572798	7604	7623	N/A	N/A	CTGAAATCTGATAAAACTA	89	Y	1838
1572836	14053	14072	2478	2497	ACATCTACCACCTTGGGAGG	42	Y	1839
1572858	12281	12300	706	725	AAAGAGTGGAGGTGGGTGGT	85	Y	1840
1572865	7014	7033	N/A	N/A	GAAAATGATTAAGACCAGAC	73	Y	1841
1572894	7731	7750	N/A	N/A	ATCTCCCTTCCCCATCACAG	82	Y	1842
1572895	11824	11843	N/A	N/A	CATCTCAAGCACCTTGTCTC	78	Y	1843
1572921	6336	6355	N/A	N/A	GTAGAGGTCAGAACCAACTG	52	Y	1844
1572944	7561	7580	N/A	N/A	AAAGCAGTCATAAAAGAACA	92	Y	1845
1572967	6832	6851	N/A	N/A	CATCATTCTGGACCTGCCAG	75	Y	1846
1572975	12935	12954	1360	1379	TGCAGAGCTACTACTAGAGG	17	Y	1847
1572986	5029	5048	N/A	N/A	AATAACAAATGGAGGCGGCG	80	Y	1848
1573015	7470	7489	N/A	N/A	GGGTCATGTTTTAGCACCAG	66	Y	1849
1573035	5096	5115	N/A	N/A	GCCCCACCCCCTGAGCCCCC	83	Y	1850
1573040	12100	12119	525	544	AGATCGGAGGGAGACTGTGG	56†	Y	1851
1573045	13149	13168	1574	1593	TGTTGGCTAAGAGGCGGCCA	72	Y	1852
1573088	15188	15207	2917	2936	ATGGTTGCGATTGCCAGGAG	20	Y	1853
1573093	6282	6301	N/A	N/A	CATCCTCCCATCATGCCCAG	65	Y	1854
1573102	6540	6559	N/A	N/A	GTCTGGGCCACCCTCACCT	80	Y	1855
1573108	18506	18525	3991	4010	CTCGCCACCTCCCCACCTCT	88	Y	1856
1573149	15941	15960	N/A	N/A	TCATGGGAAGGATACTAGAC	81	Y	1857
1573156	14078	14097	2503	2522	GGCAGACTGACTGGCATGGC	35	Y	1858
1573161	6784	6803	N/A	N/A	AGATAACAATGCAGCCCAGA	77	Y	1859
1573174	13307	13326	1732	1751	AGAGTTTCCGTGATGCTGCT	15	Y	1860
1573199	6388	6407	N/A	N/A	AAGTGCAAAGAAGCAAAAAG	88	Y	1861
1573219	6964	6983	N/A	N/A	AGAGCCCCTAAGTAAGAACA	74	Y	1862

1573245	6607	6626	N/A	N/A	TAGACACAGGTCTCCTGGCT	71	Y	1863
1573275	17864	17883	N/A	N/A	GACCAACGGATAACAAGTAC	76	Y	1864
1573302	11944	11963	N/A	N/A	CTCTTGCTCAAGCCCACCTC	76	Y	1865
1573311	9638	9657	N/A	N/A	GGTAAGCATTATTACCCTCA	54	Y	1866
1573319	13673	13692	2098	2117	TTTGTAGCCTGCTGGCGAGG	76	Y	1867
1573325	7787	7806	N/A	N/A	AAGATGACTATTTGTGATTG	66	Y	1868
1573336	6367	6386	N/A	N/A	CAACTCTACAAAAATAACA	106	Y	1869
1573352	13464	13483	1889	1908	GGCTGTAGGACACCTGGCTG	69	Y	1870
1573402	7754	7773	N/A	N/A	AGCCCTCCTAGAGAAGGGTG	95	Y	1871
1573403	7493	7512	N/A	N/A	GGATTGTGTGTCTTTCTAGA	16	Y	1872
1573413	13653	13672	2078	2097	AAGCCACGGTGGCAATGACC	91	Y	1873
1573468	11777	11796	N/A	N/A	CTTCCACCATCTCATAACCA	97	Y	1874
1573489	6712	6731	N/A	N/A	GAGAGGCCTCAGAGATCATC	101	Y	1875
1573512	7883	7902	N/A	N/A	GTTTTAAAATACTATCAACC	91	Y	1876
1573538	9174	9193	N/A	N/A	GATGTACCAGTTTTTAAGCC	57	Y	1877
1573555	7908	7927	N/A	N/A	CATTTTTTAGTTGTTATGTA	79	Y	1878
1573574	5144	5163	N/A	N/A	CACCTTCCCCGATCCTCCCGA	81	Y	1879
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	22	Y	70
1573592	11070	11089	463	482	GGTCTCCTCACTTTCACTCT	11†	Y	1880
1573632	7671	7690	N/A	N/A	GTCAGAGAAACACAGGAATG	66	Y	1881
1573699	6480	6499	N/A	N/A	GAAGAAGGCCAAAGGTTAGT	79	Y	1882
1573706	14268	14287	N/A	N/A	TCAAAACCACCCCTGCAGGC	80	Y	1883
1573710	7650	7669	N/A	N/A	ACCTGAGGAACACAGCAATC	75	Y	1884
1573724	11746	11765	N/A	N/A	ATCCTCCATCCCCAAGCCC	94	Y	1885
1573726	17307	17326	N/A	N/A	TCAGACAAACACAAGGAGGT	45	Y	1886
1573739	6439	6458	N/A	N/A	TACTCAAGAAGGGAGGCTCA	94	Y	1887
1573773	7628	7647	N/A	N/A	AGTATGCCCTTCTTTTTTAA	36	Y	1888
1573792	13548	13567	1973	1992	GGTGTGAACATGGGTAGGAC	10	Y	1889
1573810	5075	5094	N/A	N/A	GCCCTCAGGCCAGGCAGAGC	104	Y	1890
1574654	18549	18568	4034	4053	AGAGAGACCTGGTCCAAGAT	40	Y	1891
1475433	12934	12953	1359	1378	GCAGAGCTACTACTAGAGGA	22	Z	337
1572338	12162	12181	587	606	GGTCGATATCCCTAGGGTCG	20†	Z	1892
1572345	17863	17882	N/A	N/A	ACCAACGGATAACAAGTACC	63	Z	1893
1572346	15096	15115	2825	2844	CTGTAGCCACCGCACTGCCC	87	Z	1894
1572375	12028	12047	N/A	N/A	TTCCTGCTTCCCTGAGATTT	93	Z	1895
1572383	9083	9102	N/A	N/A	AGGTATCTATCTTTATCCAA	64	Z	1896
1572399	11904	11923	N/A	N/A	ACTTTCCTCACATTCTTGCC	119	Z	1897
1572400	12760	12779	1185	1204	AGTGGTTGGGCCCCCAGGCC	72	Z	1898
1572401	7649	7668	N/A	N/A	CCTGAGGAACACAGCAATCA	89	Z	1899
1572433	6605	6624	N/A	N/A	GACACAGGTCTCCTGGCTCC	79	Z	1900
1572445	12099	12118	524	543	GATCGGAGGGAGACTGTGGC	29†	Z	1901
1572446	7670	7689	N/A	N/A	TCAGAGAAACACAGGAATGT	101	Z	1902
1572454	6387	6406	N/A	N/A	AGTGCAAAGAAGCAAAAAGA	99	Z	1903
1572460	14692	14711	N/A	N/A	CCGCCCACCCAGCCACAGCC	107	Z	1904
1572475	6411	6430	N/A	N/A	TTCAAGTTTTAGAAAATGAA	101	Z	1905

1572478	8741	8760	N/A	N/A	CAGTAATTCTCACTCACCTC	59	Z	1906
1572495	7730	7749	N/A	N/A	TCTCCCTTCCCCATCACAGA	103	Z	1907
1572527	5074	5093	N/A	N/A	CCCTCAGGCCAGGCAGAGCC	99	Z	1908
1572555	13306	13325	1731	1750	GAGTTTCCGTGATGCTGCTG	8	Z	1909
1572564	14158	14177	N/A	N/A	CCCTGCTACTCCCTCTCTCG	94	Z	1910
1572569	15939	15958	N/A	N/A	ATGGGAAGGATACTAGACTA	88	Z	1911
1572628	5384	5403	N/A	N/A	GCCCCCAACCCAGGCTCCG	93	Z	1912
1572704	17306	17325	N/A	N/A	CAGACAAACACAAGGAGGTC	89	Z	1913
1572721	7627	7646	N/A	N/A	GTATGCCCTTCTTTTTTAAT	43	Z	1914
1572729	7906	7925	N/A	N/A	TTTTTTAGTTGTTATGTAGA	71	Z	1915
1572750	11943	11962	N/A	N/A	TCTTGCTCAAGCCACCTCT	88	Z	1916
1572782	6963	6982	N/A	N/A	GAGCCCCAAGTAAGAACAG	87	Z	1917
1572785	6438	6457	N/A	N/A	ACTCAAGAAGGGAGGCTCAA	91	Z	1918
1572872	13672	13691	2097	2116	TTGTAGCCTGCTGGCGAGGA	64	Z	1919
1572882	13995	14014	2420	2439	GGGTCTCATACTCCTCAGCC	66	Z	1920
1572900	13148	13167	1573	1592	GTTGGCTAAGAGGCGGCCAT	80	Z	1921
1572998	6335	6354	N/A	N/A	TAGAGGTGAGAACCAACTGC	79	Z	1922
1573023	7603	7622	N/A	N/A	TGAAATCTGATAAAAACTAG	95	Z	1923
1573081	6281	6300	N/A	N/A	ATCCTCCCATCATGCCCAGG	81	Z	1924
1573089	12362	12381	787	806	AGTGGGTGTACAGAAGGAT	10	Z	1925
1573125	7753	7772	N/A	N/A	GCCCTCCTAGAGAAGGGTGT	100	Z	1926
1573129	6366	6385	N/A	N/A	AACTCTACAAAAAATAACAT	100	Z	1927
1573133	12526	12545	951	970	GGGCCCCCCTGATGAGGC	70	Z	1928
1573143	13915	13934	2340	2359	GGTGGCAGCGATGGCAGGCC	111	Z	1929
1573150	5300	5319	N/A	N/A	TCTCCTATCCATTCTGCCTT	92	Z	1930
1573155	12280	12299	705	724	AAGAGTGGAGGTGGGTGGTA	112	Z	1931
1573163	18505	18524	3990	4009	TCGCCACCTCCCCACCTCTG	98	Z	1932
1573171	5027	5046	N/A	N/A	TAACAAATGGAGGCGGCGGC	88	Z	1933
1573193	11776	11795	N/A	N/A	TTCCACCATCTCATAACCAC	99	Z	1934
1573200	6739	6758	N/A	N/A	AAGCCTTCTGAGAATCCGGG	53	Z	1935
1573221	8828	8847	N/A	N/A	GCCTACCCATGTATTCTATT	39	Z	1936
1573232	12057	12076	N/A	N/A	AAGGGAAGACTCATTTTTTC	117	Z	1937
1573291	13547	13566	1972	1991	GTGTGAACATGGGTAGGACC	13	Z	1938
1573324	12461	12480	886	905	ACCAGTGCCCCCAGGATAGA	56	Z	1939
1573330	7821	7840	N/A	N/A	AAGAGGAAAACAATCTTAAA	108	Z	1940
1573334	13461	13480	1886	1905	TGTAGGACACCTGGCTGTGA	46	Z	1941
1573392	7371	7390	N/A	N/A	CACCTTCATTACCTTGCTTT	55	Z	1942
1573426	14077	14096	2502	2521	GCAGACTGACTGGCATGGCT	36	Z	1943
1573459	6831	6850	N/A	N/A	ATCATTCTGGACCTGCCAGA	88	Z	1944
1573461	9522	9541	N/A	N/A	TGTGCGTGACTTCAAAGCCC	46	Z	1945
1573474	11878	11897	N/A	N/A	CTAGCAGCCAGTCTTGTTTC	91	Z	1946
1573487	7560	7579	N/A	N/A	AAGCAGTCATAAAAGAACAA	108	Z	1947
1573511	13652	13671	2077	2096	AGCCACGGTGGCAATGACCG	85	Z	1948
1573516	11745	11764	N/A	N/A	TCCTCCATCCCCCAAGCCCT	93	Z	1949
1573527	6910	6929	N/A	N/A	GAAGGAATACAGTGGAGTCA	64	Z	1950

1573572	7469	7488	N/A	N/A	GGTCATGTTTTAGCACCAGC	59	Z	1951
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	20	Z	70
1573594	7423	7442	N/A	N/A	AACATAATTACAGAGCACC	67	Z	1952
1573608	9172	9191	N/A	N/A	TGTACCAGTTTTTAAGCCTA	28	Z	1953
1573619	7882	7901	N/A	N/A	TTTTAAATACTATCAACCA	108	Z	1954
1573627	5095	5114	N/A	N/A	CCCCACCCCTGAGCCCCCG	113	Z	1955
1573629	6539	6558	N/A	N/A	TCCTGGGCCACCTCACCTG	102	Z	1956
1573637	6479	6498	N/A	N/A	AAGAAGGCCAAAGGTTAGTT	79	Z	1957
1573683	14240	14259	N/A	N/A	GCTGCGGGCCTCACTGGCCA	100	Z	1958
1573734	7785	7804	N/A	N/A	GATGACTATTTGTGATTGGT	16	Z	1959
1573754	5143	5162	N/A	N/A	ACCTCCCGATCCTCCCGAA	105	Z	1960
1573757	7492	7511	N/A	N/A	GATTGTGTGTCTTTCTAGAC	40	Z	1961
1573760	11823	11842	N/A	N/A	ATCTCAAGCACCTTGTCTCT	109	Z	1962
1573762	6710	6729	N/A	N/A	GAGGCCTCAGAGATCATCTC	73	Z	1963
1573795	7013	7032	N/A	N/A	AAAATGATTAAGACCAGACT	84	Z	1964
1573815	11069	11088	462	481	GTCTCCTCACTTTCACTCTC	15†	Z	1965
1573817	6783	6802	N/A	N/A	GATAACAATGCAGCCCAGAC	77	Z	1966
1574655	18545	18564	4030	4049	AGACCTGGTCCAAGATTCTG	45	Z	1967
1572369	11903	11922	N/A	N/A	CTTTCCTCACATTCTTGGCT	98	AA	1968
1572394	12027	12046	N/A	N/A	TCCTGCTTCCCTGAGATTTG	105	AA	1969
1572457	9082	9101	N/A	N/A	GGTATCTATCTTTATCCAAA	29	AA	1970
1572463	6962	6981	N/A	N/A	AGCCCCTAAGTAAGAACAGG	102	AA	1971
1572486	12525	12544	950	969	GGCCCCCCTGATGAGGCA	82	AA	1972
1572490	15091	15110	2820	2839	GCCACCGCACTGCCCGGTTT	109	AA	1973
1572506	7559	7578	N/A	N/A	AGCAGTCATAAAAGAACAAG	85	AA	1974
1572510	7905	7924	N/A	N/A	TTTTTAGTTGTTATGTAGAC	59	AA	1975
1572539	9171	9190	N/A	N/A	GTACCAGTTTTTAAGCCTAT	7	AA	1976
1572560	12732	12751	1157	1176	AGGCTGATGCATTGTTGAGG	12	AA	1977
1572565	12279	12298	704	723	AGAGTGGAGGTGGGTGGTAG	112	AA	1978
1572576	11822	11841	N/A	N/A	TCTCAAGCACCTTGTCTCTA	96	AA	1979
1572579	7012	7031	N/A	N/A	AAATGATTAAGACCAGACTG	75	AA	1980
1572581	13305	13324	1730	1749	AGTTTCCGTGATGCTGCTGC	6	AA	1981
1572583	14076	14095	2501	2520	CAGACTGACTGGCATGGCTG	42	AA	1982
1572602	11775	11794	N/A	N/A	TCCACCATCTCATAACCACC	89	AA	1983
1572605	5142	5161	N/A	N/A	CCTTCCCGATCCTCCCGAAA	110	AA	1984
1572624	8740	8759	N/A	N/A	AGTAATTCTCACTCACCTCC	88	AA	1985
1572626	5094	5113	N/A	N/A	CCCACCCCTGAGCCCCCGG	67	AA	1986
1572629	4975	4994	N/A	N/A	GGGAGCCGCAGGCCGGAGCC	92	AA	1987
1572672	14691	14710	N/A	N/A	CGCCACCCAGCCACAGCCC	103	AA	1988
1572673	6386	6405	N/A	N/A	GTGCAAAGAAGCAAAAAGAC	108	AA	1989
1572686	7820	7839	N/A	N/A	AGAGGAAAACAATCTTAAAC	88	AA	1990
1572692	6592	6611	N/A	N/A	TGGCTCCTGTTCTATAGTAT	79	AA	1991
1572699	12460	12479	885	904	CCAGTGCCCCCAGGATAGAG	40	AA	1992
1572732	12932	12951	1357	1376	AGAGCTACTACTAGAGGATG	31	AA	1993
1572745	15938	15957	N/A	N/A	TGGGAAGGATACTAGACTAT	90	AA	1994

1572763	5073	5092	N/A	N/A	CCTCAGGCCAGGCAGAGCCC	103	AA	1995
1572788	6431	6450	N/A	N/A	AAGGGAGGCTCAAAGAGGAA	81	AA	1996
1572792	6334	6353	N/A	N/A	AGAGGTCAGAACCAACTGCC	95	AA	1997
1572816	7881	7900	N/A	N/A	TTTAAAATACTATCAACCAA	97	AA	1998
1572838	12152	12171	577	596	CCTAGGGTCTGCTGCTGCCAT	16†	AA	1999
1572839	13147	13166	1572	1591	TTGGCTAAGAGGCGGCCATA	92	AA	2000
1572841	5383	5402	N/A	N/A	CCCCCAACCCCAGGCTCCGG	92	AA	2001
1572873	12056	12075	N/A	N/A	AGGGAAGACTCATTTTTTCT	107	AA	2002
1572893	7491	7510	N/A	N/A	ATTGTGTGTCTTTCTAGACC	45	AA	2003
1572950	18537	18556	4022	4041	TCCAAGATTCTGTGCGCTTT	23	AA	2004
1572966	5299	5318	N/A	N/A	CTCCTATCCATTCTGCCTTC	70	AA	2005
1572973	7669	7688	N/A	N/A	CAGAGAAACACAGGAATGTA	96	AA	2006
1573009	11942	11961	N/A	N/A	CTTGCTCAAGCCCACCTCTT	90	AA	2007
1573069	13458	13477	1883	1902	AGGACACCTGGCTGTGAGGT	49	AA	2008
1573196	6830	6849	N/A	N/A	TCATTCTGGACCTGCCAGAC	83	AA	2009
1573251	17236	17255	N/A	N/A	ACAGGCTGAGCCCTACTGGA	99	AA	2010
1573267	6909	6928	N/A	N/A	AAGGAATACAGTGGAGTCAC	69	AA	2011
1573301	6365	6384	N/A	N/A	ACTCTACAAAAATAACATA	97	AA	2012
1573337	13651	13670	2076	2095	GCCACGGTGGCAATGACCGT	97	AA	2013
1573385	6410	6429	N/A	N/A	TCAAGTTTTAGAAAATGAAA	103	AA	2014
1573387	7728	7747	N/A	N/A	TCCCTTCCCCATCACAGAAC	98	AA	2015
1573393	6782	6801	N/A	N/A	ATAACAATGCAGCCCAGACC	93	AA	2016
1573409	7752	7771	N/A	N/A	CCCTCCTAGAGAAGGGTGTC	101	AA	2017
1573430	11744	11763	N/A	N/A	CCTCCATCCCCCAAGCCCTT	107	AA	2018
1573441	18464	18483	3949	3968	CTTCTGTCTGTCCCTCCCTC	54	AA	2019
1573447	14123	14142	N/A	N/A	CGTCCCCTTTCCAGGCCAC	85	AA	2020
1573454	12091	12110	516	535	GGAGACTGTGGCCGAGGGAG	8‡	AA	2021
1573465	8824	8843	N/A	N/A	ACCCATGTATTCTATTCTGA	50	AA	2022
1573470	6738	6757	N/A	N/A	AGCCTTCTGAGAATCCGGGA	73	AA	2023
1573486	13546	13565	1971	1990	TGTGAACATGGGTAGGACCC	18	AA	2024
1573509	13994	14013	2419	2438	GGTCTCATACTCCTCAGCCG	72	AA	2025
1573517	7602	7621	N/A	N/A	GAAATCTGATAAAAACTAGC	111	AA	2026
1573522	7369	7388	N/A	N/A	CCTTCATTACCTTGCTTTAT	38	AA	2027
1573548	7626	7645	N/A	N/A	TATGCCCTTCTTTTTTAATC	73	AA	2028
1573553	6538	6557	N/A	N/A	CCTGGGCCACCCTCACCTGG	98	AA	2029
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	22	AA	70
1573595	7774	7793	N/A	N/A	GTGATTGGTGTATTTTGCC	5	AA	2030
1573601	7648	7667	N/A	N/A	CTGAGGAACACAGCAATCAT	70	AA	2031
1573643	12361	12380	786	805	GTGGGTGTCACAGAAGGATG	36	AA	2032
1573648	6280	6299	N/A	N/A	TCCTCCCATCATGCCCAGGT	93	AA	2033
1573655	9521	9540	N/A	N/A	GTCGGTGACTTCAAAGCCCA	85	AA	2034
1573656	6709	6728	N/A	N/A	AGGCCTCAGAGATCATCTCA	87	AA	2035
1573670	6478	6497	N/A	N/A	AGAAGGCCAAAGGTTAGTTG	82	AA	2036
1573714	17859	17878	N/A	N/A	ACGGATAACAAGTACCTGCT	97	AA	2037
1573753	13914	13933	2339	2358	GTGGCAGCGATGGCAGGCCT	103	AA	2038

1573781	14239	14258	N/A	N/A	CTGCGGGCCTCACTGGCCAC	96	AA	2039
1573797	11068	11087	461	480	TCTCCTCACTTTCACTCTCT	10†	AA	2040
1573811	13671	13690	2096	2115	TGTAGCCTGCTGGCGAGGAA	69	AA	2041
1573821	7422	7441	N/A	N/A	ACTAATATTACAGAGCACCT	91	AA	2042
1573854	7468	7487	N/A	N/A	GTCATGTTTTAGCACCAGCC	21	AA	382
1573866	11877	11896	N/A	N/A	TAGCAGCCAGTCTTGTTTCC	104	AA	2043
1572351	5372	5391	N/A	N/A	AGGCTCCGGAACCCGTGTTC	89	AB	2044
1572421	5072	5091	N/A	N/A	CTCAGGCCAGGCAGAGCCCG	93	AB	2045
1572437	7668	7687	N/A	N/A	AGAGAAACACAGGAATGTAC	91	AB	2046
1572487	14233	14252	N/A	N/A	GCCTCACTGGCCACTAGGCC	95	AB	2047
1572509	14100	14119	N/A	N/A	CGCCCCACCTGGCCGCTCAC	70	AB	2048
1572514	13650	13669	2075	2094	CCACGGTGGCAATGACCGTG	90	AB	2049
1572529	14919	14938	N/A	N/A	ACAGCCGAATGCCAAAATGC	95	AB	2050
1572550	12150	12169	575	594	TAGGGTCGCTGCTGCCATCA	8†	AB	2051
1572570	7421	7440	N/A	N/A	CTAATATTACAGAGCACCTA	88	AB	2052
1572582	12360	12379	785	804	TGGGTGTCACAGAAGGATGG	34	AB	2053
1572604	6385	6404	N/A	N/A	TGCAAAGAAGCAAAAAGACA	104	AB	2054
1572662	7726	7745	N/A	N/A	CCTTCCCCATCACAGAACCT	79	AB	2055
1572666	14690	14709	N/A	N/A	GCCCCACCCAGCCACAGCCCC	89	AB	2056
1572675	6589	6608	N/A	N/A	CTCCTGTTCTATAGTATTTC	63	AB	2057
1572676	5093	5112	N/A	N/A	CCACCCCCTGAGCCCCCGGC	84	AB	2058
1572695	6477	6496	N/A	N/A	GAAGGCCAAAGGTTAGTTGA	85	AB	2059
1572762	7751	7770	N/A	N/A	CCTCCTAGAGAAGGGTGTCC	74	AB	2060
1572772	4974	4993	N/A	N/A	GGAGCCGCAGGCCGGAGCCC	103	AB	2061
1572778	13304	13323	1729	1748	GTTTCCGTGATGCTGCTGCT	8	AB	2062
1572795	6279	6298	N/A	N/A	CCTCCCATCATGCCAGGTG	88	AB	2063
1572820	6829	6848	N/A	N/A	CATTCTGGACCTGCCAGACT	87	AB	2064
1572833	7595	7614	N/A	N/A	GATAAAACTAGCAATGAGA	98	AB	2065
1572864	11066	11085	459	478	TCCTCACTTTCACTCTCTGA	18†	AB	2066
1572868	13912	13931	2337	2356	GGCAGCGATGGCAGGCCTGA	88	AB	2067
1572885	12090	12109	515	534	GAGACTGTGGCCGAGGGAGT	22†	AB	2068
1572902	6333	6352	N/A	N/A	GAGGTCAGAACCAACTGCCA	82	AB	2069
1572943	6961	6980	N/A	N/A	GCCCCCTAAGTAAGAACAGGA	98	AB	2070
1572945	12731	12750	1156	1175	GGCTGATGCATTGTTGAGGG	4	AB	2071
1572994	6737	6756	N/A	N/A	GCCTTCTGAGAATCCGGGAC	68	AB	2072
1573001	7490	7509	N/A	N/A	TTGTGTGTCTTTCTAGACCT	53	AB	2073
1573002	12459	12478	884	903	CAGTGCCCCCAGGATAGAGC	31	AB	2074
1573014	12524	12543	949	968	GCCCCCACTGATGAGGCAG	85	AB	2075
1573022	11876	11895	N/A	N/A	AGCAGCCAGTCTTGTTTCCC	84	AB	2076
1573051	6708	6727	N/A	N/A	GGCCTCAGAGATCATCTCAT	83	AB	2077
1573112	12278	12297	703	722	GAGTGGAGGTGGGTGGTAGG	94	AB	2078
1573113	12055	12074	N/A	N/A	GGGAAGACTCATTTTTTCTC	91	AB	2079
1573124	8739	8758	N/A	N/A	GTAATTCTCACTCACCTCCA	72	AB	2080
1573141	15821	15840	N/A	N/A	GCAATCTCAGGAAAGGTTCA	85	AB	2081
1573144	11941	11960	N/A	N/A	TTGCTCAAGCCACCTCTTA	95	AB	2082

1573170	11773	11792	N/A	N/A	CACCATCTCATAACCACCAC	91	AB	2083
1573182	7904	7923	N/A	N/A	TTTTAGTTGTTATGTAGACT	68	AB	2084
1573223	7773	7792	N/A	N/A	TGATTGGTGTATTTTGGCA	17	AB	2085
1573236	11821	11840	N/A	N/A	CTCAAGCACCTTGTCTCTAC	90	AB	2086
1573237	7819	7838	N/A	N/A	GAGGAAAACAATCTTAAACA	70	AB	2087
1573286	11743	11762	N/A	N/A	CTCCATCCCCCAAGCCCTTG	102	AB	2088
1573287	18536	18555	4021	4040	CCAAGATTCTGTGCGCTTTC	12	AB	359
1573292	13146	13165	1571	1590	TGGCTAAGAGGCGGCCATAG	87	AB	2089
1573308	17195	17214	N/A	N/A	AGGACAGGAGATTACAGTCA	100	AB	2090
1573321	9170	9189	N/A	N/A	TACCAGTTTTTAAGCCTATC	12	AB	2091
1573372	8822	8841	N/A	N/A	CCATGTATTCTATTCTGAGT	62	AB	2092
1573373	6908	6927	N/A	N/A	AGGAATACAGTGGAGTCACA	81	AB	2093
1573397	6409	6428	N/A	N/A	CAAGTTTTAGAAAATGAAAG	99	AB	2094
1573420	12026	12045	N/A	N/A	CCTGCTTCCCTGAGATTTGG	95	AB	2095
1573433	9080	9099	N/A	N/A	TATCTATCTTTATCCAAATC	94	AB	2096
1573434	14075	14094	2500	2519	AGACTGACTGGCATGGCTGG	52	AB	2097
1573457	7880	7899	N/A	N/A	TTAAATACTATCAACCAAA	102	AB	2098
1573492	7647	7666	N/A	N/A	TGAGGAACACAGCAATCATA	60	AB	2099
1573520	7368	7387	N/A	N/A	CTTCATTACCTTGCTTTATT	43	AB	2100
1573524	13993	14012	2418	2437	GTCTCATACTCCTCAGCCGG	56	AB	2101
1573536	5298	5317	N/A	N/A	TCCTATCCATTCTGCCTTCG	93	AB	2102
1573545	13670	13689	2095	2114	GTAGCCTGCTGGCGAGGAAG	57	AB	2103
1573554	6534	6553	N/A	N/A	GGCCACCCTCACCTGGGATG	95	AB	2104
1573579	17823	17842	N/A	N/A	CCAGCTCCTTTACATACAAA	79	AB	2105
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTCAGGAT	19	AB	70
1573609	5141	5160	N/A	N/A	CTTCCCGATCCTCCCGAAAC	101	AB	2106
1573633	18462	18481	3947	3966	TCTGTCTGTCCCTCCCTCCC	60	AB	2107
1573651	6781	6800	N/A	N/A	TAACAATGCAGCCCAGACCA	85	AB	2108
1573657	7558	7577	N/A	N/A	GCAGTCATAAAAGAACAAGT	79	AB	2109
1573672	12929	12948	1354	1373	GCTACTACTAGAGGATGAAT	20	AB	2110
1573712	9517	9536	N/A	N/A	GTGACTTCAAAGCCCATGCT	41	AB	2111
1573718	13456	13475	1881	1900	GACACCTGGCTGTGAGGTGG	79	AB	2112
1573723	11902	11921	N/A	N/A	TTTCCTCACATTCTTGGCTG	82	AB	2113
1573735	13545	13564	1970	1989	GTGAACATGGGTAGGACCCT	20	AB	2114
1573756	7625	7644	N/A	N/A	ATGCCCTTCTTTTTTAATCA	48	AB	2115
1573793	7467	7486	N/A	N/A	TCATGTTTTAGCACCAGCCT	40	AB	2116
1573812	6363	6382	N/A	N/A	TCTACAAAAAATAACATAAT	100	AB	2117
1573845	6430	6449	N/A	N/A	AGGGAGGCTCAAAGAGGAAT	86	AB	2118
1573856	7011	7030	N/A	N/A	AATGATTAAGACCAGACTGG	72	AB	2119
1572355	7750	7769	N/A	N/A	CTCCTAGAGAAGGGTGTCCA	95	AC	2120
1572409	11899	11918	N/A	N/A	CCTCACATTCTTGGCTGCTC	96	AC	2121
1572424	6473	6492	N/A	N/A	GCCAAAGGTTAGTTGAGGGA	71	AC	2122
1572458	17682	17701	N/A	N/A	CAGCTCTCCTATTCCCATGC	103	AC	2123
1572484	5139	5158	N/A	N/A	TCCCGATCCTCCCGAAACCC	93	AC	2124
1572606	6905	6924	N/A	N/A	AATACAGTGGAGTCACAAGC	84	AC	2125

1572635	5297	5316	N/A	N/A	CCTATCCATTCTGCCTTCGC	92	AC	2126
1572636	9507	9526	N/A	N/A	AGCCCATGCTCTTTCTTCTA	61	AC	2127
1572643	7594	7613	N/A	N/A	ATAAAAACTAGCAATGAGAA	95	AC	2128
1572711	14917	14936	N/A	N/A	AGCCGAATGCCAAAATGCCT	94	AC	2129
1572713	12695	12714	1120	1139	GGGAGGCAGGTTTCGGTGTCA	32	AC	2130
1572734	6533	6552	N/A	N/A	GCCACCCTCACCTGGGATGG	89	AC	2131
1572786	7466	7485	N/A	N/A	CATGTTTTAGCACCAGCCTA	55	AC	2132
1572804	11940	11959	N/A	N/A	TGCTCAAGCCCACCTCTTAC	93	AC	2133
1572829	12149	12168	574	593	AGGGTCGCTGCTGCCATCAT	4†	AC	2134
1572830	11742	11761	N/A	N/A	TCCATCCCCCAAGCCCTTGG	97	AC	2135
1572855	5092	5111	N/A	N/A	CACCCCTGAGCCCCGGCC	102	AC	2136
1572861	9169	9188	N/A	N/A	ACCAGTTTTTAAGCCTATCC	19	AC	465
1572877	6588	6607	N/A	N/A	TCCTGTTCTATAGTATTTCC	34	AC	2137
1572879	13544	13563	1969	1988	TGAACATGGGTAGGACCCTT	77	AC	2138
1572889	13303	13322	1728	1747	TTTCCGTGATGCTGCTGCTG	16	AC	2139
1572897	5071	5090	N/A	N/A	TCAGGCCAGGCAGAGCCCGC	107	AC	2140
1572955	7010	7029	N/A	N/A	ATGATTAAGACCAGACTGGG	78	AC	2141
1572963	14687	14706	N/A	N/A	CACCCAGCCACAGCCCCGCA	116	AC	2142
1572992	7772	7791	N/A	N/A	GATTGGTGTATTTTTGCCAG	62	AC	2143
1573000	12523	12542	948	967	CCCCCACTGATGAGGCAGC	95	AC	2144
1573016	6828	6847	N/A	N/A	ATTCTGGACCTGCCAGACTA	111	AC	2145
1573060	6332	6351	N/A	N/A	AGGTCAGAACCAACTGCCAA	106	AC	2146
1573063	11820	11839	N/A	N/A	TCAAGCACCTTGTCTCTACC	100	AC	2147
1573067	12054	12073	N/A	N/A	GGAAGACTCATTTTTTCTCT	99	AC	2148
1573114	11772	11791	N/A	N/A	ACCATCTCATAACCACCACT	96	AC	2149
1573119	7040	7059	N/A	N/A	GCACTGCCATTACCTTACTT	63	AC	2150
1573127	5361	5380	N/A	N/A	CCCGTGTCTGGTCCTTTGG	62	AC	2151
1573166	12457	12476	882	901	GTGCCCCCAGGATAGAGCTG	78	AC	2152
1573172	9065	9084	N/A	N/A	AAATCCCTATAGCCAGCTGT	49	AC	2153
1573189	13633	13652	2058	2077	GTGGAAAGGGTAGCCGAAGA	83	AC	2154
1573194	7622	7641	N/A	N/A	CCCTTCTTTTTTAATCACCT	35	AC	2155
1573205	6429	6448	N/A	N/A	GGGAGGCTCAAAGAGGAATT	91	AC	2156
1573216	14074	14093	2499	2518	GACTGACTGGCATGGCTGGG	24	AC	2157
1573241	16828	16847	N/A	N/A	TGGGCAAAAGAAAAAAGGA	108	AC	2158
1573250	14232	14251	N/A	N/A	CCTCACTGGCCACTAGGCCT	117	AC	2159
1573261	7903	7922	N/A	N/A	TTTAGTTGTTATGTAGACTG	43	AC	2160
1573273	13436	13455	1861	1880	GGGCAGGTGTGCTGGCCCTG	86	AC	2161
1573274	12025	12044	N/A	N/A	CTGCTCCCTGAGATTGCGG	108	AC	2162
1573282	7489	7508	N/A	N/A	TGTGTGTCTTTCTAGACCTG	47	AC	2163
1573293	12089	12108	514	533	AGACTGTGGCCGAGGGAGTT	46†	AC	2164
1573294	6780	6799	N/A	N/A	AACAATGCAGCCCAGACCAG	96	AC	2165
1573312	4973	4992	N/A	N/A	GAGCCGCAGGCCGAGCCCG	109	AC	2166
1573316	7667	7686	N/A	N/A	GAGAAACACAGGAATGTACC	99	AC	2167
1573328	6384	6403	N/A	N/A	GCAAAGAAGCAAAAAGACAA	88	AC	2168
1573343	8734	8753	N/A	N/A	TCTCACTCACCTCCACGGAA	75	AC	2169

1573347	6278	6297	N/A	N/A	CTCCCATCATGCCCAGGTGG	107	AC	2170
1573354	8794	8813	N/A	N/A	TGCTAGGTAAACGGCATGTC	71	AC	2171
1573408	7813	7832	N/A	N/A	AACAATCTTAAACAAAAAGC	101	AC	2172
1573437	6408	6427	N/A	N/A	AAGTTTTAGAAAATGAAAGA	114	AC	2173
1573448	18459	18478	3944	3963	GTCTGTCCCTCCCTCCCCCA	71	AC	2174
1573540	6736	6755	N/A	N/A	CCTTCTGAGAATCCGGGACC	103	AC	2175
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	20	AC	70
1573591	14098	14117	N/A	N/A	CCCCACCTGGCCGCTCACCT	93	AC	2176
1573593	7646	7665	N/A	N/A	GAGGAACACAGCAATCATAG	46	AC	2177
1573599	15774	15793	N/A	N/A	CCATAGGAATGAAAGAGCCC	111	AC	2178
1573600	11873	11892	N/A	N/A	AGCCAGTCTTGTTCCTCGCC	96	AC	2179
1573607	13911	13930	2336	2355	GCAGCGATGGCAGGCCTGAG	67	AC	2180
1573612	6707	6726	N/A	N/A	GCCTCAGAGATCATCTCATC	95	AC	2181
1573624	12247	12266	672	691	CCCTGGGACAGGCCAGAAGA	105	AC	2182
1573680	7725	7744	N/A	N/A	CTTCCCCATCACAGAACCTG	100	AC	2183
1573695	13669	13688	2094	2113	TAGCCTGCTGGCGAGGAAGC	86	AC	2184
1573705	7557	7576	N/A	N/A	CAGTCATAAAGAACAAGTA	106	AC	2185
1573768	13989	14008	2414	2433	CATACTCCTCAGCCGGCTCC	105	AC	2186
1573772	12885	12904	1310	1329	GAGCAGAAGAGGAAGCAGGA	84	AC	2187
1573789	7420	7439	N/A	N/A	TAATATTACAGAGCACCTAC	90	AC	2188
1573818	18535	18554	4020	4039	CAAGATTCTGTGCGCTTTCT	26	AC	2189
1573823	11065	11084	458	477	CCTCACTTTCCTCTCTGAG	18†	AC	2190
1573825	13145	13164	1570	1589	GGCTAAGAGGCGGCCATAGG	65	AC	2191
1573827	7879	7898	N/A	N/A	TAAAATACTATCAACCAAAA	108	AC	2192
1573828	6362	6381	N/A	N/A	CTACAAAAAATAACATAATA	107	AC	2193
1573858	12337	12356	762	781	TCAAAGCTAGCCTCTGGCTG	98	AC	2194
1573859	6960	6979	N/A	N/A	CCCCTAAGTAAGAACAGGAA	99	AC	2195
1441008	6587	6606	N/A	N/A	CCTGTTCTATAGTATTTCCC	27	AD	483
1572343	6383	6402	N/A	N/A	CAAAGAAGCAAAAAGACAAC	92	AD	2196
1572344	9168	9187	N/A	N/A	CCAGTTTTTAAGCCTATCCT	17	AD	2197
1572352	13301	13320	1726	1745	TCCGTGATGCTGCTGCTGCT	27	AD	2198
1572378	12088	12107	513	532	GACTGTGGCCGAGGGAGTTC	42†	AD	2199
1572397	7621	7640	N/A	N/A	CCTTCTTTTTTAATCACCTG	18	AD	2200
1572413	12140	12159	565	584	GCTGCCATCATCATTAGGC	48†	AD	2201
1572439	18534	18553	4019	4038	AAGATTCTGTGCGCTTTCTG	32	AD	2202
1572521	12336	12355	761	780	CAAAGCTAGCCTCTGGCTGT	68	AD	2203
1572522	7039	7058	N/A	N/A	CACTGCCATTACCTTACTTT	68	AD	2204
1572525	7488	7507	N/A	N/A	GTGTGTCTTTCTAGACCTGG	43	AD	2205
1572528	5295	5314	N/A	N/A	TATCCATTCTGCCTTCGCCC	64	AD	2206
1572577	13144	13163	1569	1588	GCTAAGAGGCGGCCATAGGG	30	AD	2207
1572608	5091	5110	N/A	N/A	ACCCCTGAGCCCCCGGCC	92	AD	2208
1572637	13668	13687	2093	2112	AGCCTGCTGGCGAGGAAGCC	103	AD	2209
1572678	7645	7664	N/A	N/A	AGGAACACAGCAATCATAGT	68	AD	2210
1572694	6779	6798	N/A	N/A	ACAATGCAGCCCAGACCAGC	89	AD	2211
1572710	12694	12713	1119	1138	GGAGGCAGGTTCTGGTGTAC	32	AD	2212

1572715	7009	7028	N/A	N/A	TGATTAAGACCAGACTGGGT	81	AD	2213
1572719	6428	6447	N/A	N/A	GGAGGCTCAAAGAGGAATTC	90	AD	2214
1572744	7556	7575	N/A	N/A	AGTCATAAAAGAACAAGTAA	98	AD	2215
1572756	7771	7790	N/A	N/A	ATTGGTGTATTTTGCCAGC	72	AD	2216
1572767	14096	14115	N/A	N/A	CCACCTGGCCGCTCACCTGG	99	AD	2217
1572780	7419	7438	N/A	N/A	AATATTACAGAGCACCTACT	87	AD	2218
1572808	14603	14622	N/A	N/A	GGCAGTGACGCACTCACCAC	104	AD	2219
1572846	13988	14007	2413	2432	ATACTCCTCAGCCGGCTCCT	89	AD	2220
1572862	5070	5089	N/A	N/A	CAGGCCAGGCAGAGCCCGCA	82	AD	2221
1572871	11939	11958	N/A	N/A	GCTCAAGCCCACCTCTTACC	101	AD	2222
1572899	6733	6752	N/A	N/A	TCTGAGAATCCGGGACCTTC	66	AD	2223
1572911	7902	7921	N/A	N/A	TTAGTTGTTATGTAGACTGG	38	AD	2224
1572922	12522	12541	947	966	CCCCCACTGATGAGGCAGCC	89	AD	2225
1572925	6472	6491	N/A	N/A	CCAAAGGTTAGTTGAGGGAA	86	AD	2226
1572927	11771	11790	N/A	N/A	CCATCTCATAACCACCACTT	103	AD	2227
1572941	16827	16846	N/A	N/A	GGGCAAAAAGAAAAAAGGAA	96	AD	2228
1572953	6331	6350	N/A	N/A	GGTCAGAACCAACTGCCAAA	66	AD	2229
1572987	6501	6520	N/A	N/A	AGCCATTTCTACAAGGTCAG	52	AD	2230
1573043	11064	11083	457	476	CTCACTTTCCTCTCTGAGA	38†	AD	2231
1573052	18456	18475	3941	3960	TGTCCTCCCTCCCCCACTC	85	AD	2232
1573055	7812	7831	N/A	N/A	ACAATCTTAAACAAAAAGCA	84	AD	2233
1573076	13910	13929	2335	2354	CAGCGATGGCAGGCCTGAGG	76	AD	2234
1573084	13543	13562	1968	1987	GAACATGGGTAGGACCCTTG	46	AD	2235
1573092	5113	5132	N/A	N/A	CCGACTCTCCTCGGCGGGCC	99	AD	2236
1573136	4953	4972	N/A	N/A	GGCGGGACAGAACCCCGCGG	83	AD	2237
1573178	11872	11891	N/A	N/A	GCCAGTCTTGTTTCCCGCCT	87	AD	2238
1573187	8791	8810	N/A	N/A	TAGGTAAACGGCATGTCCAT	68	AD	2239
1573195	7593	7612	N/A	N/A	TAAAACTAGCAATGAGAAG	105	AD	2240
1573201	6827	6846	N/A	N/A	TTCTGGACCTGCCAGACTAA	97	AD	2241
1573238	11819	11838	N/A	N/A	CAAGCACCTTGTCTTACCC	94	AD	2242
1573295	14073	14092	2498	2517	ACTGACTGGCATGGCTGGGT	29	AD	2243
1573368	7724	7743	N/A	N/A	TTCCCCATCACAGAACCTGT	86	AD	2244
1573386	12232	12251	657	676	GAAGATGAGTCAGAGTCATT	44	AD	2245
1573395	13632	13651	2057	2076	TGGAAAGGGTAGCCGAAGAG	79	AD	2246
1573400	7749	7768	N/A	N/A	TCCTAGAGAAGGGTGTCCAT	78	AD	2247
1573411	11741	11760	N/A	N/A	CCATCCCCCAAGCCCTTGGT	98	AD	2248
1573412	6904	6923	N/A	N/A	ATACAGTGGAGTCACAAGCT	68	AD	2249
1573444	9054	9073	N/A	N/A	GCCAGCTGTATTCATTTGCA	47	AD	2250
1573469	14860	14879	N/A	N/A	CGGCCCCCGCTCCCGAATAT	95	AD	2251
1573471	15740	15759	N/A	N/A	GAAGGTGGCCCCAAAGGGCC	106	AD	2252
1573501	7465	7484	N/A	N/A	ATGTTTTAGCACCAGCCTAC	81	AD	2253
1573503	7878	7897	N/A	N/A	AAAATACTATCAACCAAAAA	85	AD	2254
1573551	6361	6380	N/A	N/A	TACAAAAAATAACATAATAA	99	AD	2255
1573552	12052	12071	N/A	N/A	AAGACTCATTTTTCTCTTT	96	AD	2256
1573577	11897	11916	N/A	N/A	TCACATTCTTGCTGCTCCC	102	AD	2257

1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	22	AD	70
1573618	13435	13454	1860	1879	GGCAGGTGTGCTGGCCCTGG	69	AD	2258
1573649	9506	9525	N/A	N/A	GCCCATGCTCTTTCTTCTAT	36	AD	2259
1573685	12873	12892	1298	1317	AAGCAGGAGGCAGAGAGTGG	90	AD	2260
1573700	6706	6725	N/A	N/A	CCTCAGAGATCATCTCATCT	72	AD	2261
1573709	6277	6296	N/A	N/A	TCCCATCATGCCCAGGTGGA	92	AD	2262
1573730	11985	12004	N/A	N/A	TTCCCCTCACAGCACACTGT	95	AD	2263
1573741	7666	7685	N/A	N/A	AGAAACACAGGAATGTACCT	90	AD	2264
1573745	17681	17700	N/A	N/A	AGCTCTCCTATTCCCATGCC	78	AD	2265
1573790	8692	8711	N/A	N/A	GGGTGAGTCTAACCTTTCCA	76	AD	2266
1573791	6407	6426	N/A	N/A	AGTTTTAGAAAATGAAAGAA	99	AD	2267
1573803	14228	14247	N/A	N/A	ACTGGCCACTAGGCCTGGAC	98	AD	2268
1573824	5360	5379	N/A	N/A	CCGTGTTCTGGTCCTTTGGA	70	AD	2269
1573833	6959	6978	N/A	N/A	CCCTAAGTAAGAACAGGAAA	89	AD	2270
1573846	12455	12474	880	899	GCCCCCAGGATAGAGCTGTG	60	AD	2271
1510556	11057	11076	450	469	TCACTCTCTGAGATCTCCTC	54	AE	2272
1572335	8638	8657	N/A	N/A	GCTGGGACAGAGCCTATCTT	120	AE	2273
1572342	6471	6490	N/A	N/A	CAAAGGTTAGTTGAGGGAAA	120	AE	2274
1572387	6732	6751	N/A	N/A	CTGAGAATCCGGGACCTTCA	67	AE	2275
1572485	6276	6295	N/A	N/A	CCCATCATGCCCAGGTGGAG	105	AE	2276
1572503	14094	14113	N/A	N/A	ACCTGGCCGCTCACCTGGCA	136	AE	2277
1572533	8790	8809	N/A	N/A	AGGTAAACGGCATGTCCATA	43	AE	2278
1572547	6775	6794	N/A	N/A	TGCAGCCCAGACCAGCAGAT	104	AE	2279
1572610	7008	7027	N/A	N/A	GATTAAGACCAGACTGGGTT	97	AE	2280
1572622	13631	13650	2056	2075	GGAAAGGGTAGCCGAAGAGG	80	AE	2281
1572634	6875	6894	N/A	N/A	GGGCTCGCAGGCTAAATTTTC	89	AE	2282
1572645	13300	13319	1725	1744	CCGTGATGCTGCTGCTGCTG	8	AE	2283
1572691	9047	9066	N/A	N/A	GTATTCATTTGCACTTGTTT	11	AE	2284
1572697	15739	15758	N/A	N/A	AAGGTGGCCCCAAAGGGCCA	136	AE	2285
1572712	13667	13686	2092	2111	GCCTGCTGGCGAGGAAGCCA	81	AE	2286
1572722	6826	6845	N/A	N/A	TCTGGACCTGCCAGACTAAC	125	AE	2287
1572774	6427	6446	N/A	N/A	GAGGCTCAAAGAGGAATTCA	97	AE	2288
1572796	13434	13453	1859	1878	GCAGGTGTGCTGGCCCTGGT	81	AE	2289
1572812	14196	14215	N/A	N/A	CGTGCTTTTCTAAACACTA	100	AE	2290
1572856	6500	6519	N/A	N/A	GCCATTCTACAAGGTCAGG	39	AE	2291
1572892	11938	11957	N/A	N/A	CTCAAGCCCACCTCTTACCA	129	AE	2292
1572901	13987	14006	2412	2431	TACTCCTCAGCCGGCTCCTG	102	AE	2293
1572909	12335	12354	760	779	AAAGCTAGCCTCTGGCTGTC	74	AE	2294
1572926	7664	7683	N/A	N/A	AAACACAGGAATGTACCTGA	98	AE	2295
1572931	6586	6605	N/A	N/A	CTGTTCTATAGTATTTCCCC	18	AE	2296
1572964	5090	5109	N/A	N/A	CCCCCTGAGCCCCCGGCCCT	138	AE	2297
1572997	7036	7055	N/A	N/A	TGCCATTACCTTACTTTAAA	59	AE	2298
1573012	14072	14091	2497	2516	CTGACTGGCATGGCTGGGTA	71	AE	2299
1573019	9505	9524	N/A	N/A	CCCATGCTCTTTCTTCTATA	41	AE	2300
1573020	7620	7639	N/A	N/A	CTTCTTTTTTAATCACCTGA	60	AE	2301

1573027	12123	12142	548	567	GGCTCCGCCCCGTCCAAGCTA	53†	AE	2302
1573033	7592	7611	N/A	N/A	AAAAACTAGCAATGAGAAGC	107	AE	2303
1573037	7748	7767	N/A	N/A	CCTAGAGAAGGGTGTCCATC	83	AE	2304
1573046	11770	11789	N/A	N/A	CATCTCATAACCACCACTTT	100	AE	2305
1573071	7901	7920	N/A	N/A	TAGTTGTTATGTAGACTGGT	32	AE	2306
1573075	11896	11915	N/A	N/A	CACATTCTTGGCTGCTCCCT	108	AE	2307
1573083	12454	12473	879	898	CCCCCAGGATAGAGCTGTGG	100	AE	2308
1573094	12219	12238	644	663	AGTCATTCTCCACACTTCCA	35	AE	2309
1573165	7877	7896	N/A	N/A	AAATACTATCAACCAAAAAA	103	AE	2310
1573179	13143	13162	1568	1587	CTAAGAGGCGGCCATAGGGA	40	AE	104
1573212	7770	7789	N/A	N/A	TTGGTGTATTTTGGCAGCC	90	AE	2311
1573226	5294	5313	N/A	N/A	ATCCATTCTGCCTTCGCCCCG	109	AE	2312
1573239	7464	7483	N/A	N/A	TGTTTTAGCACCAGCCTACA	92	AE	2313
1573257	7811	7830	N/A	N/A	CAATCTTAAACAAAAAGCAC	140	AE	2314
1573320	13874	13893	2299	2318	GGGCCCAGGTCCCACGGTGG	82	AE	2315
1573327	7487	7506	N/A	N/A	TGTGTCCTTCTAGACCTGGG	52	AE	2316
1573338	6405	6424	N/A	N/A	TTTTAGAAAATGAAAGAAAG	130	AE	2317
1573384	5359	5378	N/A	N/A	CGTGTCTGGTCCTTTGGAG	55	AE	2318
1573394	6705	6724	N/A	N/A	CTCAGAGATCATCTCATCTA	73	AE	2319
1573424	16825	16844	N/A	N/A	GCAAAAGAAAAAAGGAAGC	117	AE	2320
1573429	7418	7437	N/A	N/A	ATATTACAGAGCACCTACTC	124	AE	2321
1573438	5112	5131	N/A	N/A	CGACTCTCCTCGGCGGGCCC	127	AE	2322
1573449	12521	12540	946	965	CCCCACTGATGAGGCAGCCC	105	AE	2323
1573455	14856	14875	N/A	N/A	CCCCGCTCCCGAATATTTGC	92	AE	2324
1573477	11870	11889	N/A	N/A	CAGTCTTGTTTCCCGCCTGT	110	AE	2325
1573480	7555	7574	N/A	N/A	GTCATAAAAGAACAAGTAAT	129	AE	2326
1573481	17680	17699	N/A	N/A	GCTCTCCTATTCCCATGCCC	123	AE	2327
1573502	12051	12070	N/A	N/A	AGACTCATTTTTCTCTTTT	72	AE	2328
1573535	12693	12712	1118	1137	GAGGCAGGTTCCGGTGTCACA	13	AE	258
1573557	11984	12003	N/A	N/A	TCCCCTCACAGCACACTGTT	120	AE	2329
1573566	13542	13561	1967	1986	AACATGGGTAGGACCCTTGA	94	AE	2330
1573576	6360	6379	N/A	N/A	ACAAAAAATAACATAATAAG	114	AE	2331
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTTCAGGAT	23	AE	70
1573642	7723	7742	N/A	N/A	TCCCCATCACAGAACCTGTT	76	AE	2332
1573654	12087	12106	512	531	ACTGTGGCCGAGGGAGTTCC	41†	AE	2333
1573658	9167	9186	N/A	N/A	CAGTTTTTAAGCCTATCCTC	57	AE	2334
1573668	18533	18552	4018	4037	AGATTCTGTGCGCTTTCTGT	40	AE	2335
1573674	6382	6401	N/A	N/A	AAAGAAGCAAAAAGACAAC	85	AE	2336
1573696	11817	11836	N/A	N/A	AGCACCTTGTCTCTACCCAC	95	AE	2337
1573711	14600	14619	N/A	N/A	AGTGACGCACTCACCACGCT	127	AE	2338
1573713	12843	12862	1268	1287	CCAGAGTTGGGCCCTTCTCT	118	AE	2339
1573725	18455	18474	3940	3959	GTCCCTCCCTCCCCACTCT	99	AE	2340
1573731	6958	6977	N/A	N/A	CCTAAGTAAGAACAGGAAAA	138	AE	2341
1573778	5069	5088	N/A	N/A	AGGCCAGGCAGAGCCCGCAG	122	AE	2342
1573787	11740	11759	N/A	N/A	CATCCCCCAAGCCCTTGGTT	128	AE	2343

1573788	6330	6349	N/A	N/A	GTCAGAACCAACTGCCAAAA	81	AE	2344
1573820	4948	4967	N/A	N/A	GACAGAACCCCGCGGGCCCG	107	AE	2345
1573861	7644	7663	N/A	N/A	GGAACACAGCAATCATAGTA	83	AE	2346
1475694	6584	6603	N/A	N/A	GTTCTATAGTATTTCCCTG	17	AF	528
1572337	7769	7788	N/A	N/A	TGGTGTATTTTGGCAGCCC	67	AF	2347
1572423	13630	13649	2055	2074	GAAAGGGTAGCCGAAGAGGT	40	AF	263
1572450	11895	11914	N/A	N/A	ACATTCTTGGCTGCTCCCTA	102	AF	2348
1572451	11769	11788	N/A	N/A	ATCTCATAACCACCACCTTTA	127	AF	2349
1572492	12841	12860	1266	1285	AGAGTTGGGCCCTTCTCTGG	92	AF	2350
1572592	18450	18469	3935	3954	TCCCTCCCCCACTCTCTGTC	117	AF	2351
1572593	13433	13452	1858	1877	CAGGTGTGCTGGCCCTGGTG	61	AF	2352
1572600	7663	7682	N/A	N/A	AACACAGGAATGTACCTGAG	106	AF	2353
1572607	6499	6518	N/A	N/A	CCATTTCTACAAGGTCAGGG	40	AF	2354
1572612	11050	11069	443	462	CTGAGATCTCCTCACTCCGA	30	AF	2355
1572614	14195	14214	N/A	N/A	GTGCTTTTCTAAAACACTAC	102	AF	2356
1572620	17652	17671	N/A	N/A	TAGGCACCTCCTCATCCCTC	109	AF	2357
1572651	18531	18550	4016	4035	ATTCTGTGCGCTTTCTGTCC	35	AF	2358
1572664	5089	5108	N/A	N/A	CCCCTGAGCCCCCGGCCCTC	126	AF	2359
1572708	6359	6378	N/A	N/A	CAAAAAATAACATAATAAGG	137	AF	2360
1572718	7643	7662	N/A	N/A	GAACACAGCAATCATAGTAT	39	AF	2361
1572728	8789	8808	N/A	N/A	GGTAAACGGCATGTCCATAT	17	AF	306
1572738	7896	7915	N/A	N/A	GTTATGTAGACTGGTTTTAA	10	AF	2362
1572753	11983	12002	N/A	N/A	CCCCTCACAGCACACTGTTG	112	AF	2363
1572783	6404	6423	N/A	N/A	TTTAGAAAATGAAAGAAAGT	117	AF	2364
1572814	14071	14090	2496	2515	TGACTGGCATGGCTGGGTAC	46	AF	2365
1572827	6731	6750	N/A	N/A	TGAGAATCCGGGACCTTCAG	58	AF	2366
1572831	5293	5312	N/A	N/A	TCCATTCTGCCTTCGCCCGG	128	AF	2367
1572840	12692	12711	1117	1136	AGGCAGGTTCGGTGTACAT	5	AF	2368
1572866	9164	9183	N/A	N/A	TTTTTAAGCCTATCCTCCTA	98	AF	2369
1572867	12216	12235	641	660	CATTCTCCACACTTCCAGGG	49	AF	2370
1572938	4947	4966	N/A	N/A	ACAGAACCCCGCGGGCCCGG	98	AF	2371
1572940	8628	8647	N/A	N/A	AGCCTATCTTCTGAACTTTC	83	AF	2372
1572981	15586	15605	3315	3334	CCCAGGGCCGCCACCCTTTC	93	AF	2373
1572999	6329	6348	N/A	N/A	TCAGAACCAACTGCCAAAAG	72	AF	2374
1573007	5358	5377	N/A	N/A	GTGTTCTGGTCCTTTGGAGC	57	AF	2375
1573008	13141	13160	1566	1585	AAGAGGCGGCCATAGGGAGG	95	AF	2376
1573032	6825	6844	N/A	N/A	CTGGACCTGCCAGACTAACA	69	AF	2377
1573049	16461	16480	N/A	N/A	AAACCCAAAGCTACAGGGCC	123	AF	2378
1573086	6381	6400	N/A	N/A	AAGAAGCAAAAAGACAACTC	85	AF	2379
1573098	6426	6445	N/A	N/A	AGGCTCAAAGAGGAATTCAA	78	AF	2380
1573099	13541	13560	1966	1985	ACATGGGTAGGACCCTTGAG	74	AF	2381
1573126	14570	14589	2712	2731	TCGCGCTCCTTCTCGCGCTC	119	AF	2382
1573135	6763	6782	N/A	N/A	CAGCAGATAACGATGCACTG	82	AF	2383
1573169	13986	14005	2411	2430	ACTCCTCAGCCGGCTCCTGT	76	AF	2384
1573227	14092	14111	N/A	N/A	CTGGCCGCTCACCTGGCAGA	118	AF	2385

1573247	6695	6714	N/A	N/A	ATCTCATCTATAGCCCCTTC	61	AF	2386
1573263	7007	7026	N/A	N/A	ATTAAGACCAGACTGGGTTG	114	AF	2387
1573264	13221	13240	1646	1665	GTGTTGAGACTGGTGGGTGG	71	AF	2388
1573300	7876	7895	N/A	N/A	AATACTATCAACCAAAAAA	127	AF	2389
1573313	12050	12069	N/A	N/A	GACTCATTTTTTCTCTTTTC	114	AF	2390
1573344	12453	12472	878	897	CCCCAGGATAGAGCTGTGGG	87	AF	2391
1573356	12086	12105	511	530	CTGTGGCCGAGGGAGTTCCT	11†	AF	2392
1573357	6465	6484	N/A	N/A	TTAGTTGAGGGAAGAGGAA	121	AF	2393
1573374	6957	6976	N/A	N/A	CTAAGTAAGAACAGGAAAAG	135	AF	2394
1573379	14855	14874	N/A	N/A	CCCGCTCCCGAATATTTGCC	108	AF	2395
1573390	7034	7053	N/A	N/A	CCATTACCTTACTTTAAAAA	124	AF	2396
1573410	12122	12141	547	566	GCTCCGCCCGTCCAAGCTAT	43†	AF	2397
1573421	7591	7610	N/A	N/A	AAAAGTAGCAATGAGAAGCT	92	AF	2398
1573431	5111	5130	N/A	N/A	GACTCTCCTCGGCGGGCCCC	137	AF	2399
1573478	7554	7573	N/A	N/A	TCATAAAAGAACAAGTAATC	127	AF	2400
1573547	13666	13685	2091	2110	CCTGCTGGCGAGGAAGCCAC	129	AF	2401
1573558	13843	13862	2268	2287	TTGAAGGTCCCTGGGCCTGC	132	AF	2402
1573561	11813	11832	N/A	N/A	CCTTGCTCTACCCACAGCT	86	AF	2403
1573565	7417	7436	N/A	N/A	TATTACAGAGCACCTACTCT	108	AF	2404
1573580	6870	6889	N/A	N/A	CGCAGGCTAAATTTCAGGAT	26	AF	70
1573590	7747	7766	N/A	N/A	CTAGAGAAGGGTGTCCATCT	42	AF	2405
1573628	7463	7482	N/A	N/A	GTTTTAGCACCAGCCTACAC	120	AF	2406
1573631	7618	7637	N/A	N/A	TCTTTTTTAATCACCTGAAA	116	AF	2407
1573635	11937	11956	N/A	N/A	TCAAGCCCACCTCTTACCAT	132	AF	2408
1573664	11869	11888	N/A	N/A	AGTCTTGTTTCCCGCCTGTA	77	AF	2409
1573665	7486	7505	N/A	N/A	GTGTCTTTCTAGACCTGGGT	23	AF	2410
1573736	12334	12353	759	778	AAGCTAGCCTCTGGCTGTCG	62	AF	2411
1573759	7810	7829	N/A	N/A	AATCTTAAACAAAAAGCACA	169	AF	2412
1573764	9504	9523	N/A	N/A	CCATGCTCTTTCTTCTATAC	30	AF	2413
1573775	12520	12539	945	964	CCCCTGATGAGGCAGCCCC	85	AF	2414
1573782	5068	5087	N/A	N/A	GGCCAGGCAGAGCCCGCAGT	87	AF	2415
1573805	6040	6059	N/A	N/A	ACCATAGCAACACAGTGGCA	76	AF	2416
1573807	11739	11758	N/A	N/A	ATCCCCAAGCCCTTGTTTT	119	AF	2417
1573844	7722	7741	N/A	N/A	CCCCATCACAGAACCTGTTC	137	AF	2418
1573857	9043	9062	N/A	N/A	TCATTTGCACTTGTTGTAT	49	AF	2419
1573863	6874	6893	N/A	N/A	GGCTCGCAGGCTAAATTTCA	128	AF	2420

Example 6: Dose-dependent inhibition of human ATN1 in A431 cells by modified oligonucleotides, *in vitro*

Modified oligonucleotides selected from the examples above were tested at various doses in A431 cells. A431 cells plated at a density of 10,000 cells per well were treated using free uptake with various 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 ATN1 RNA levels were measured by quantitative real-time RT-PCR. Human ATN1 primer-probe set RTS40640 (described herein above) was used to measure RNA levels as described above. ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the

table below as percent ATN1 RNA, relative to the amount of ATN1 RNA in untreated control cells (% UTC). The values marked with a “†” indicate that the modified oligonucleotide is complementary to the amplicon region of the primer probe set.

The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the table below.

Table 9

Dose-dependent reduction of human ATN1 RNA in A431 cells by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)				IC ₅₀ (μM)
	63 nM	250 nM	1000 nM	4000 nM	
1441008	56	28	15	9	0.06
1475375	62	25	11	5	0.08
1475384	57	28	12	5	0.07
1475398	31	14	6	4	<0.063
1475409	72	51	23	14	0.25
1475415	69	43	27	16	0.21
1475422	67	50	27	15	0.22
1475423	78	48	42	12	0.35
1475433	45	19	6	4	<0.063
1475496	95	59	31	16	0.51
1475507	34	16	6	3	<0.063
1475517	72	44	24	15	0.22
1475532	81	54	26	12	0.34
1475542	70	38	24	12	0.18
1475547	71	43	22	10	0.20
1475569	67	46	26	16	0.20
1475572	46	21	10	5	<0.063
1475574	69	43	22	12	0.19
1475584	67	33	15	9	0.13

Table 10

Dose-dependent reduction of human ATN1 RNA in A431 cells by modified oligonucleotides

Compound No.	ATN1 RNA (% UTC)				IC ₅₀ (μM)
	63 nM	250 nM	1000 nM	4000 nM	
1441008	62	33	17	11	0.10
1475594	60	32	13	7	0.09
1475628	72	49	25	13	0.24
1475631	73	52	23	17	0.27
1475658	69	44	15	9	0.18
1475661	67	32	14	7	0.12
1475665	62	37	22	11	0.12
1475681	46†	33†	24†	21†	<0.063†

1475683	65	33	15	6	0.12
1475689	63	39	19	8	0.13
1475694	56	27	12	7	0.06
1475697	75	49	29	15	0.29
1475699	65	38	17	10	0.14
1475708	75	44	23	12	0.23
1475715	76	42	27	17	0.25
1475763	78	53	42	27	0.50
1475770	89	52	30	14	0.40
1475787	66	37	19	11	0.14
1475801	72	41	17	10	0.19

Example 7: Dose-dependent inhibition of human ATN1 in A431 cells by 5-10-5 MOE gapmers, *in vitro*

Modified oligonucleotides selected from the examples above were tested at various doses in A431 cells. A431 cells plated at a density of 10,000 cells per well were treated using free uptake with various 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 ATN1 RNA levels were measured by quantitative real-time RT-PCR. Human ATN1 primer-probe set RTS40640 (described herein above) was used to measure RNA levels as described above. ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA, relative to the amount of ATN1 RNA in untreated control cells (% UTC).

The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the table below.

Table 11

Dose-dependent reduction of human ATN1 RNA in A431 cells by 5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages

Compound No.	ATN1 RNA (% UTC)					IC ₅₀ (μM)
	23 nM	94 nM	375 nM	1500 nM	6000 nM	
1143346	76	41	19	8	4	0.08
1143347	101	64	38	20	10	0.30
1143378	98	62	49	29	22	0.44
1143426	90	67	44	26	20	0.36
1143642	92	89	90	84	75	>6
1143654	88	62	41	25	13	0.27

Example 8: Dose-dependent inhibition of human ATN1 in A431 cells by 5-10-5 MOE gapmers, *in vitro*

Modified oligonucleotides complementary to a human ATN1 RNA were designed and tested for their effects on ATN1 RNA *in vitro*. The modified oligonucleotides in the tables below are 5-10-5 MOE gapmers with mixed PS/PO internucleoside linkages. The modified oligonucleotides in the table below are 20 nucleosides in length, wherein the sugar motif for the modified oligonucleotides is (from 5' to 3'): eeeeeeeeeeeeeeeeeee; wherein "e" represents a 2'-MOE ribosyl sugar moiety, and each "d" represents a 2'-deoxyribosyl sugar moiety. The internucleoside linkage motif for the modified oligonucleotides is (from 5' to 3'): sooooooooooooo; wherein each "s" represents a phosphorothioate internucleoside linkage, and each "o" represents a phosphodiester internucleoside linkage. Each cytosine residue is a 5-methylcytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the target nucleic acid sequence. Each modified oligonucleotide listed in the tables below is 100% complementary to SEQ ID NO: 1 (GenBank Accession No. NC_000012.12 truncated from nucleosides 6923463 to 6943321).

Modified oligonucleotides were tested at various doses in A431 cells. A431 cells plated at a density of 10,000 cells per well were treated using free uptake with various 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 ATN1 RNA levels were measured by quantitative real-time RT-PCR. Human ATN1 primer-probe set RTS40640 (described herein above) was used to measure RNA levels as described above. ATN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Reduction of ATN1 RNA is presented in the table below as percent ATN1 RNA, relative to the amount of ATN1 RNA in untreated control cells (% UTC). The half maximal inhibitory concentration (IC₅₀) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in Excel and is also presented in the table below. "N.C." indicates that a value was not calculated. Each table represents a separate experiment.

Table 12

Dose-dependent reduction of human ATN1 RNA in A431 cells by 5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence (5' to 3')	ATN1 RNA (% UTC)					IC ₅₀ (μM)	SEQ ID NO
				23 nM	94 nM	375 nM	1500 nM	6000 nM		
1440996	12049	12068	ACTCATTTTTTCTCTTTTCC	108	115	113	97	112	>6	2421
1440997	11761	11780	ACCACCACTTTAACCATCCT	104	97	92	106	84	>6	2422
1440998	11758	11777	ACCACTTTAACCATCCTCCA	93	95	99	85	69	>6	2423
1440999	2115	2134	GCACTCACTTTACCACTCCA	97	107	97	104	118	>6	2424
1441000	8666	8685	TTCACAATTTACTTAGAATC	93	102	86	76	74	>6	2425
1441001	8667	8686	CTTCAACAATTTACTTAGAAT	104	98	86	71	67	>6	2426
1441002	11385	11404	TCTGCATTTTCCTTAAGATT	95	77	85	68	60	>6	2427
1441003	7038	7057	ACTGCCATTACCTTACTTTA	93	71	61	36	22	0.62	2428

1441004	12048	12067	CTCATTTTTTCTCTTTTCCT	112	109	111	101	100	>6	2429
1441005	9081	9100	GTATCTATCTTTATCCAAAT	88	82	66	54	31	1.49	2430
1441006	10666	10685	ACTGTTCTTTACATTGCACC	98	103	98	49	90	N.C.	2431
1441007	7361	7380	ACCTTGCTTTATTTTATTTA	84	78	66	39	29	0.86	2432
1441008	6587	6606	CCTGTTCTATAGTATTTCCC	91	64	39	20	12	0.27	483
1441009	8267	8286	TAGTTTTCTTTTTTTTCCT	79	77	76	52	36	2.15	2433
1441010	7624	7643	TGCCCTTCTTTTTTAATCAC	89	110	71	67	43	5.53	2434

Table 13

Dose-dependent reduction of human ATN1 RNA in A431 cells by 5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages

Compound No.	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	Sequence (5' to 3')	ATN1 (% UTC)					IC50 (μM)	SEQ ID NO
				23 nM	94 nM	375 nM	1500 nM	6000 nM		
1441011	11910	11929	TTTCTCACTTTCCTCACATT	102	114	104	115	101	>6	2435
1441012	6697	6716	TCATCTCATCTATAGCCCCT	96	85	81	61	42	4.08	2436
1441013	6585	6604	TGTTCTATAGTATTTCCCCT	93	83	49	33	15	0.52	2437
1441014	12047	12066	TCATTTTTTCTCTTTTCCTT	110	103	109	85	137	>6	2438
1441015	10564	10583	CTCTCATTTTAACTCACCGA	105	111	101	113	116	>6	2439
1441016	9496	9515	TTTCTTCTATACTTTGCTGT	82	75	57	27	15	0.41	2440
1441017	11208	11227	TGGCCTTTCTCTTATGTCCC	99	88	115	82	86	>6	2441
1441018	11727	11746	CTTGGTTTTTATACCACTTC	104	93	84	78	71	>6	2442
1441019	1019	1038	CCTTGAAGTTCCTCCCACTT	98	114	108	107	104	>6	2443

Example 9: Tolerability of modified oligonucleotides complementary to human ATN1 in wild-type mice, 3-hour study

Modified oligonucleotides described above were tested in wild-type mice to assess the tolerability of the oligonucleotides.

Wild-type female C57BL/6 mice (Taconic Biosciences) each received a single ICV dose of 700 μg of modified oligonucleotide. Each treatment group consisted of 4 mice. A group of 4 mice received PBS as a negative control. At 3 hours post-injection, mice were evaluated according to seven 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). After all 7 criteria were evaluated, the scores were summed for each mouse and averaged within each treatment group.

Table 14

Tolerability scores in wild-type mice

Compound No.	3 hr. FOB
PBS	0.00
1143346	6.25
1143347	6.00
1143378	6.00
1143426	4.25
1143642	3.00
1143654	1.25
1440996	0.00
1440997	0.00
1440998	0.00
1440999	0.00
1441000	0.00
1441001	0.00
1441002	0.00
1441003	1.00
1441004	0.00
1441005	0.00
1441006	1.00
1441007	4.00
1441008	2.00
1441009	0.00
1441010	0.00
1441011	0.00
1441012	1.75
1441013	2.75
1441014	0.00
1441015	0.00
1441016	1.00
1441017	0.00
1441018	0.00
1441019	1.00

Table 15

Tolerability scores in wild-type mice

Compound No.	3 hr. FOB
PBS	0.00
1475542	1.00
1475572	0.50

1475787	2.00
1572705	2.25
1573262	2.75

Example 10: Tolerability of modified oligonucleotides complementary to human ATN1 in rats, 3-hour study

Modified oligonucleotides described above were tested in rats to assess the tolerability of the oligonucleotides. Sprague Dawley rats (Envigo) 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 4 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 (the functional observational battery score or FOB). 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.

Table 16

Tolerability scores in rats

Compound No.	3 hr. FOB
PBS	0.00
1475542	0.75
1475572	0.75
1475787	1.50
1572705	2.50
1573262	3.50

Example 11: Activity of modified oligonucleotides complementary to human ATN1 in transgenic mice, 2 weeks

Modified oligonucleotides from the above examples were analyzed for their effects on ATN1 mRNA in humanized ATN1 mice where human *ATN1* gene is knocked into mouse *Atn1* locus via CRISPR/Cas-9-mediated gene editing on a C57BL/6NTac background. The line was generated by Taconic, and is called C57BL/6NTac-*Atn1*^{em7219(ATN1)Tac}, but is herein referred to as ATN1 transgenic mice.

ATN1 transgenic mice were divided into groups of 2 mice. Each mouse received a single ICV bolus of 300 µg. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Two weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue, spinal cord, and brainstem for quantitative real-time RTPCR analysis of RNA expression of ATN1 using human primer probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to mouse PPIA. Mouse PPIA was amplified using primer probe set m_cyclo24 (forward sequence TCGCCGCTTGCTGCA, designated herein as SEQ ID NO: 9; reverse sequence ATCGGCCGTGATGTGCA, designated herein as SEQ ID NO: 10; probe sequence CCATGGTCAACCCACCGTGTTTC, designated herein as SEQ ID NO: 11). Results are presented as percent human

ATN1 RNA relative to the amount of human ATN1 RNA in PBS treated animals, (% control). The values marked with a “†” indicate that the modified oligonucleotide is complementary to the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of the modified oligonucleotides complementary to the amplicon region.

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Table 17

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100	100	100
1441013	60	68	73
1441016	54	81	53
1475375	62	50	59
1475398	43	46	39
1475415	62	74	79
1475435	101†	116†	124†
1475477	71	78	58
1475505	45	90	64
1475543	122	130	92
1475631	42	39	37
1475678	81	80	83
1475699	40	20	40
1475770	59	53	75
1572395	79	70	67
1572397	50	31	42
1572464	68	79	80
1572544	55	24	59
1572677	78	66	95
1572691	44	63	64
1572794	71	89	82
1572825	57	34	67
1573010	88	100	87
1573172	62	54	60
1573262	29	32	38
1573297	92	95	117

Table 18

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100 ±	100±	100±
1143643	90	54	85
1143671	119	110	106
1441008	59	36	50
1475485	75	81	77
1475530	86	46	53
1475531	109	75	84
1475542	57	52	33
1475572	28	11	29
1475574	135	81	118
1475584	83	54	84
1475592	64†	31†	58†
1475597	62	38	64
1475602	109	73	79
1475616	75	35	63
1475627	101	63	91±
1475632	92	67	94
1475635	80	55	99
1475682	99	60	74
1475683	51	41	56
1475755	105	111	105
1475787	29	19	28
1475793	83	75	85
1475798	60	48	63
1475800	78	86	128
1475813	57	32	77
1572344	53	40	52
1572392	66	27	59
1572457	48	26	50
1572705	46±	38±	49±
1572771	110	43	83
1572847	76	64	86
1573054	93	60	74

1573115	73	51	59
1573235	61	58	68
1573479	68	23	48

‡ indicates fewer than 2 treatment samples available or fewer than 4 PBS samples available

Table 19

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord RTS40640	Cortex RTS40640	Brainstem RTS40640
PBS	100	100	100
1143654	45	45	24
1475393	58	90	58
1475409	78	82	56
1475465	52	77	51
1475496	68	83	58
1475521	93	102	68
1475582	36	52	29
1475628	65	81	34
1475651	45	70	49
1475661	49	53	48
1475676	45	51	42
1475681	107†	104†	88†
1475685	24†	44†	29†
1475689	45	60	44
1475693	87	71	72
1475697	45	74	52
1475712	114	106	88
1475715	30	33	34
1475718	98†	88†	77†
1475797	91	75	55
1475801	101	104	77
1475810	112	43	58
1572644	21†	39†	28†
1573194	47	51	20
1573797	42†	38†	22†

Table 20

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord RTS40640	Cortex RTS40640	Brainstem RTS40640
PBS	100	100	100
1143641	43	86	57
1475370	88	128	90
1475385	68	127	80
1475391	69†	108†	91†
1475400	51†	56†	62†
1475469	80	116	94
1475503	65†	87†	82†
1475563	63	110	85
1475634	39	61	48
1475751	46	40	46
1475763	45	73	65
1475774	57	84	72
1572383	55	60	72
1572539	41	58	43
1572603	42	58	45
1572806	59	91	59
1573206	39	74	46
1573221	55	59	51
1573712	62	83	54
1573767	48	82	39
1573804	64	97	66
1573823	36†	101†	59†
1573854	52	49	61

Example 12: Activity of modified oligonucleotides complementary to human ATN1 in transgenic mice, 8 weeks

Modified oligonucleotides from the above examples were analyzed for their effects on ATN1 mRNA in transgenic ATN1 mice (described herein above).

ATN1 transgenic mice were divided into groups of 3-4 mice. Each mouse received a single ICV bolus of 300 µg. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Eight weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue, spinal cord, and brainstem for quantitative real-time RTPCR analysis of RNA expression of ATN1 using human primer probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to mouse PPIA. Mouse PPIA was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human ATN1 RNA relative to the amount of ATN1 RNA in PBS treated animals, (% control). The values marked with a “†” indicate that the modified

oligonucleotide is complementary to the amplicon region of the primer probe set. Additional assays may be used to measure the potency and efficacy of the modified oligonucleotides complementary to the amplicon region.

Table 21

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100	100	100
1475542	52	69	66
1475572	26	17	26
1475787	37	27	36
1572705	64	63	64
1573262	30	45	38

Table 22

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100	100	100
1475699	38	59	42
1475715	39	61	42
1572397	31	51	39
1572457	66	99	68
1572644	38‡	50‡	40‡
1573194	34	73	35
1573479	42	49	47

Table 23

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100	100	100
1475813	82	88	81
1572392	53	73	67
1572544	45	49	45
1572825	40‡	55‡	45‡

‡ indicates fewer than 4 samples available

Example 13: Activity of modified oligonucleotides complementary to human ATN1 in transgenic mice, 16 weeks

Modified oligonucleotides from the above examples were analyzed for their effects on ATN1 mRNA in transgenic ATN1 mice (described herein above).

ATN1 transgenic mice were divided into groups of 4 mice. Each mouse received a single ICV bolus of 300µg.

A group of 4 mice received a single ICV bolus with PBS as a negative control.

Sixteen weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue, spinal cord, and brainstem for quantitative real-time RTPCR analysis of RNA expression of ATN1 using human primer probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to mouse PPIA. Mouse PPIA was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human ATN1 RNA relative to the amount of ATN1 RNA in PBS treated animals, (% control).

Table 24

Reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	ATN1 RNA (% control)		
	Spinal Cord	Cortex	Brainstem
PBS	100‡	100‡	100‡
1475572	41	48	55
1475787	46	39	59
1573194	65	55	67

‡ indicates fewer than 4 samples available

Example 14: Potency of modified oligonucleotides complementary to human ATN1 in transgenic mice, 8 weeks

Modified oligonucleotides from the above examples were analyzed for their effects on ATN1 mRNA in transgenic ATN1 mice (described herein above).

ATN1 transgenic mice were divided into groups of 4 mice. Each mouse received a single ICV bolus of modified oligonucleotide at doses indicated in the tables below. A group of 4 mice received a single ICV bolus with PBS as a negative control.

Eight weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue, spinal cord, and brainstem for quantitative real-time RTPCR analysis of RNA expression of ATN1 using human primer probe set RTS40640 (described herein above). ATN1 RNA levels were normalized to mouse PPIA. Mouse PPIA was amplified using primer probe set m_cyclo24 (described herein above). Results are presented as percent human ATN1 RNA relative to the amount of ATN1 RNA in PBS treated animals, (% control).

The half maximal effective dose (ED₅₀) of each modified oligonucleotide was calculated using GraphPad Prism 7 software (GraphPad Software, San Diego, CA). N.C. refers to values not calculated.

Table 25

Dose-dependent percent reduction of human ATN1 RNA in ATN1 transgenic mice

Compound No.	Dose (μg)	ATN1 RNA (% control)					
		Spinal Cord	ED50 (μg)	Cortex	ED50 (μg)	Brainstem	ED50 (μg)
PBS	-	100	-	100	-	100	-
1475787	10	92	101.4	107	255.0	91	135.6
	30	72		100		74	
	100	43		77		52	
	300	32		44		39	
	700	22		20		22	

CLAIMS:

1. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of an ATN1 nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

2. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 15-2443, wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

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

an equal length portion of nucleobases 6584-6607 of SEQ ID NO: 1;
 an equal length portion of nucleobases 6865-6890 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7364-7409 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7405-7430 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7484-7514 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7621-7658 of SEQ ID NO: 1;
 an equal length portion of nucleobases 7886-7922 of SEQ ID NO: 1;
 an equal length portion of nucleobases 8763-8809 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9082-9107 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9093-9174 of SEQ ID NO: 1;
 an equal length portion of nucleobases 9483-9525 of SEQ ID NO: 1;
 an equal length portion of nucleobases 10163-10200 of SEQ ID NO: 1;
 an equal length portion of nucleobases 11033-11081 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12214-12244 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12360-12400 of SEQ ID NO: 1;
 an equal length portion of nucleobases 12929-12957 of SEQ ID NO: 1;
 an equal length portion of nucleobases 13300-13330 of SEQ ID NO: 1;
 an equal length portion of nucleobases 14061-14097 of SEQ ID NO: 1;
 an equal length portion of nucleobases 18284-18363 of SEQ ID NO: 1;
 an equal length portion of nucleobases 18658-18689 of SEQ ID NO: 1; or
 an equal length portion of nucleobase ranges disclosed in Table 1;

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

4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 50 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least

13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or 20 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 528, 2437, 2296, 483, and 2137;
 SEQ ID NOs: 1329, 1241, 1166, 459, 70, and 1116;
 SEQ ID NOs: 770, 699, 2100, 2027, 677, 1942, 606, 527, 841, 1799, 769, 716, 654, 605, 492, 876, 1719, and 799;
 SEQ ID NOs: 1626, 1557, 1486, 1412, 1337, 1251, and 1187;
 SEQ ID NOs: 948, 651, 2410, 2316, 2205, 2163, 2073, 2003, 1961, 1872, and 1782;
 SEQ ID NOs: 2200, 2155, 583, 2434, 2115, 2028, 1914, 1888, 1747, 1693, 1659, 1532, 1493, 1367, 1346, 1262, 1172, 460, and 71;
 SEQ ID NOs: 1632, 1587, 1452, 1434, 1301, 1260, 1140, 1095, 1021, 960, 2362, 2306, 2224, and 2160;
 SEQ ID NOs: 1711, 1635, 1524, 1502, 1385, 1296, 1276, 150, 228, 1093, 985, 907, 306, and 2278;
 SEQ ID NOs: 1970, 1896, 765, 694, 1801, 643, and 590;
 SEQ ID NOs: 867, 812, 464, 1288, 704, 1215, 75, 1191, 153, 231, 562, 548, 1060, 861, 834, 1029, 690, 680, 309, and 387;
 SEQ ID NOs: 625, 1359, 1244, 2440, 1150, 1091, 1032, 929, 2413, 2300, and 2259;
 SEQ ID NOs: 634, 581, 543, 863, 809, 721, 669, 157, and 235;
 SEQ ID NOs: 94, 172, 681, 250, 502, 927, 878, 792, 732, 328, 406, 2355, 573, 538, 2272, 902, 827, and 740;
 SEQ ID NOs: 779, 741, 2370, 645, 2309, 594, 499, 903, 775, and 738;
 SEQ ID NOs: 2053, 2032, 1925, 1821, 1780, 1696, 1613, 176, 254, 332, 1499, 410, 21, 99, 518, 177, and 255;
 SEQ ID NOs: 2110, 181, 1993, 259, 337, 1847, 1746, 711, and 415;
 SEQ ID NOs: 2283, 2198, 2139, 2062, 1981, 1909, 1860, 416, 1695, 1622, and 1567;
 SEQ ID NOs: 1553, 34, 1480, 112, 1331, 190, 1165, 1075, 1059, 982, 2365, 2299, 2243, 2157, 2097, 1982, 1943, and 1858;
 SEQ ID NOs: 584, 551, 887, 800, 702, 637, 591, 201, 279, 494, 357, 435, 865, 46, 124, 202, 280, and 358;
 SEQ ID NOs: 895, 764, 691, 678, 438, 49, 874, 828, 754, 127, 205, and 561; and
 SEQ ID NOs: 870, 819, 1278, 1151, 1066, 1205, 1114, 748, 304, 1771, 1732, 1595, 1526, 1508, 149, 1390, 227, 1248, 2085, 2030, 1959, 1730, 1611, 1520, 739, 665, 604, 509, 844, 152, 1457, 1387, 1297, 1216, 1188, 1097, 1016, 2284, 787, 757, 2250, 308, 386, 2153, 627, 615, 510, 905, 2197, 465, 2091, 1976, 1953, 833, 729, 666, 597, 530, 629, 613, 519, 890, 832, 1212, 689, 676, 807, 713, 664, 612, 511, 836, 777, 709, 683, 557, 983, 512, 1286, 411, 22, 100, 2074, 1992, 1939, 1825, 791, 752, 1809, 1722, 1607, 1528, 569, 537, 858, 1369, 816, 717, 659, 1109, 1014, 962, 2368, 258, 2212, 2130, 2071, 1977, 182, 1703, 1592, 1565, 1462, 1371, 1292, 1245, 1200, 1101, 996, 964, 2114, 2024, 1938, 1889, 1839, 1742, 614, 1727, 267, 839, 785, 351, 429, 761, 40, 1853, 1802, 118, 1682, 196, 1537, 1498, 1407, 1321, 679, 601, 549, 853, 547, 899, 2358, 2335, 2202, 2189, 359, 2004, and 437.

5. The oligomeric compound of any of claims 1-4, wherein the modified oligonucleotide has a nucleobase sequence that is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length portion of a ATN1 nucleic acid, wherein the ATN1 nucleic acid has the nucleobase sequence of SEQ ID NO: 1 or SEQ ID NO: 2.

6. The oligomeric compound of any of claims 1-5, wherein the modified oligonucleotide consists of 12 to 20, 12 to 25, 12 to 30, 12 to 50, 13 to 20, 13 to 25, 13 to 30, 13 to 50, 14 to 20, 14 to 25, 14 to 30, 14 to 50, 15 to 20, 15 to 25, 15 to 30, 15 to 50, 16 to 18, 16 to 20, 16 to 25, 16 to 30, 16 to 50, 17 to 20, 17 to 25, 17 to 30, 17 to 50, 18 to 20, 18 to 25, 18 to 30, 18 to 50, 19 to 20, 19 to 25, 19 to 30, 19 to 50, 20 to 25, 20 to 30, or 20 to 50 linked nucleosides.
7. The oligomeric compound of any of claims 1-6, wherein the modified oligonucleotide comprises at least one modified nucleoside.
8. The oligomeric compound of claim 7, wherein the at least one modified nucleoside comprises a modified sugar moiety.
9. The oligomeric compound of claim 8, wherein the modified sugar moiety comprises a bicyclic sugar moiety.
10. The oligomeric compound of claim 9, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂- and -O-CH(CH₃)-.
11. The oligomeric compound of any of claims 7-10, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a non-bicyclic modified sugar moiety.
12. The oligomeric compound of claim 11, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety, a 2'-OMe sugar moiety, or a 2'-F sugar moiety.
13. The oligomeric compound of any of claims 7-12, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.
14. The oligomeric compound of claim 13, wherein the sugar surrogate is selected from morpholino, modified morpholino, glycol nucleic acid (GNA), six-membered tetrahydropyran (THP), and F-hexitol nucleic acid (F-HNA).
15. The oligomeric compound of any of claims 1-14, wherein the modified oligonucleotide is a gapmer.
16. The oligomeric compound of any of claims 1-15, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.
17. The oligomeric compound of claim 16, wherein the at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.
18. The oligomeric compound of any of claims 1-17, wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.
19. The oligomeric compound of any of claims 16-18, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.
20. The oligomeric compound of any of claims 1-19, wherein at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, or 19 internucleoside linkages of the modified oligonucleotide are phosphorothioate internucleoside linkages.
21. The oligomeric compound of any of claims 1-20, wherein the modified oligonucleotide comprises an internucleoside linkage motif (from 5' to 3') selected from sosossssssssssooss and soossssssssssooss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.
22. The oligomeric compound of any of claims 1-21, wherein the modified oligonucleotide comprises at least one modified nucleobase.

23. The oligomeric compound of claim 22, wherein the modified nucleobase is a 5-methylcytosine.
24. The oligomeric compound of claim 23, wherein each cytosine is a 5-methylcytosine.
25. The oligomeric compound of any of claims 1-24, wherein the modified oligonucleotide comprises a deoxy region.
26. The oligomeric compound of claim 25, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.
27. The oligomeric compound of claim 25 or claim 26, wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.
28. The oligomeric compound of any of claims 25-27, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.
29. The oligomeric compound of any of claims 24-27, wherein the deoxy region is flanked on the 5'-side by a 5'-region consisting of 1-6 linked 5'-region nucleosides and on the 3'-side by a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein at least one nucleoside of the 5'-region comprises a modified sugar moiety; and at least one nucleoside of the 3'-region comprises a modified sugar moiety.
30. The oligomeric compound of claim 29, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.
31. The oligomeric compound of claim 29 or claim 30, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.
32. The oligomeric compound of any of claims 1-31, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 14-20, 15-17, 15-25, 16-20, 18-22, or 18-20 linked nucleosides, or a pharmaceutically acceptable salt thereof.
33. The oligomeric compound of any of claims 1-32, wherein the modified oligonucleotide consists of 10 linked nucleosides, or a pharmaceutically acceptable salt thereof.
34. The oligomeric compound of claim 32 or claim 33, which is a pharmaceutically acceptable salt comprising one or more cations selected from sodium, potassium, calcium, and magnesium.
35. The oligomeric compound of any of claims 1-34, wherein the modified oligonucleotide consists of 20 linked nucleosides.
36. The oligomeric compound of any of claims 1-35, wherein the modified oligonucleotide comprises:
a 5'-region consisting of 1-6 linked 5'-region nucleosides;
a central region consisting of 6-10 linked central region nucleosides; and
a 3'-region consisting of 1-6 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety, and
each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.
37. The oligomeric compound of any of claims 1-36, wherein the modified oligonucleotide comprises:
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety, and
each of the central region nucleosides comprises a 2'-β-D-deoxyribose sugar moiety.

38. The oligomeric compound of claim 37, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked 5'-region nucleosides;
a central region consisting of 10 linked central region nucleosides; and
a 3'-region consisting of 5 linked 3'-region nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a 2'-MOE sugar moiety, and
each of the central region nucleosides comprises a 2'- β -D-deoxyribosyl sugar moiety.
39. The oligomeric compound of any of claims 1-38, wherein the oligomeric compound consists of the
modified oligonucleotide.
40. The oligomeric compound of any of claims 1-38, wherein the oligomeric compound comprises a
conjugate group.
41. The oligomeric compound of claim 40, wherein the conjugate group comprises a conjugate moiety and
a conjugate linker.
42. The oligomeric compound of claim 41, wherein the conjugate linker is a phosphodiester linker.
43. The oligomeric compound of claim 41, wherein the conjugate linker consists of a single bond.
44. The oligomeric compound of any of claims 41-43, wherein the conjugate linker is cleavable.
45. The oligomeric compound of any of claims 41-44, wherein the conjugate linker comprises 1-3 linker-
nucleosides.
46. The oligomeric compound of any of claims 40-45, wherein the conjugate group is attached to the
modified oligonucleotide at the 5'-end of the modified oligonucleotide.
47. The oligomeric compound of any of claims 40-45, wherein the conjugate group is attached to the
modified oligonucleotide at the 3'-end of the modified oligonucleotide.
48. The oligomeric compound of any of claims 1-47, wherein the oligomeric compound comprises a
terminal group.
49. The oligomeric compound of any of claims 1-45 or 46-48, wherein the oligomeric compound does not
comprise linker-nucleosides.
50. A chirally enriched population of oligomeric compounds of any of claims 1-49, wherein the
population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside
linkage having a particular stereochemical configuration.
51. The chirally enriched population of claim 50, wherein the population is enriched for modified
oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Sp*)
configuration.
52. The chirally enriched population of claim 50, wherein the population is enriched for modified
oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the (*Rp*)
configuration.
53. The chirally enriched population of claim 50, wherein the population is enriched for modified
oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate
internucleoside linkage.

54. The chirally enriched population of claim 50, wherein the population is enriched for modified oligonucleotides having the (*Sp*) configuration at each phosphorothioate internucleoside linkage or for modified oligonucleotides having the (*Rp*) configuration at each phosphorothioate internucleoside linkage.

55. The chirally enriched population of claim 50, 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.

56. The chirally enriched population of claim 50, 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.

57. A population of oligomeric compounds of any of claims 1-49, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

58. An oligomeric duplex comprising a first oligomeric compound and a second oligomeric compound comprising a second modified oligonucleotide, wherein the first oligomeric compound is an oligomeric compound of any of claims 1-49.

59. The oligomeric duplex of claim 58, wherein the second modified oligonucleotide consists of 12 to 50 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 12 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

60. The oligomeric duplex of claim 58 or claim 59, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.

61. The oligomeric duplex of claim 60, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.

62. The oligomeric duplex of any of claims 58-61, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.

63. The oligomeric duplex of claim 62, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.

64. The oligomeric duplex of claim 63, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from -O-CH₂- and -O-CH(CH₃)-.

65. The oligomeric duplex of claim 62, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.

66. The oligomeric duplex of claim 65, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-OMe sugar moiety or a 2'-F sugar moiety.

67. The oligomeric duplex of any of claims 62-66, wherein at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate.

68. The oligomeric duplex of any of claims 58-67, wherein the second modified oligonucleotide comprises at least one modified internucleoside linkage.

69. The oligomeric duplex of claim 68, wherein the at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

70. The oligomeric duplex of claim 68, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester internucleoside linkage and a phosphorothioate internucleoside linkage.

71. The oligomeric duplex of any of claims 58-70, wherein the second modified oligonucleotide comprises at least one modified nucleobase.

72. The oligomeric duplex of claim 71, wherein the at least one modified nucleobase is 5-methylcytosine.

73. The oligomeric duplex of any of claims 58-72, wherein the second oligomeric compound comprises a conjugate group.

74. The oligomeric duplex of claim 73, wherein the conjugate group comprises a conjugate moiety and a conjugate linker.

75. The oligomeric duplex of claim 73, wherein the conjugate linker consists of a single bond.

76. The oligomeric duplex of claim 74 or claim 75, wherein the conjugate linker is cleavable.

77. The oligomeric duplex of any of claims 74-76, wherein the conjugate linker comprises 1-3 linker-nucleosides.

78. The oligomeric duplex of any of claims 74-77, wherein the conjugate linker is a phosphodiester linker.

79. The oligomeric duplex of any of claims 73-78, wherein the conjugate group is attached to the 5'-end of the second modified oligonucleotide.

80. The oligomeric duplex of any of claims 73-78, wherein the conjugate group is attached to the 3'-end of the second modified oligonucleotide.

81. The oligomeric duplex of any of claims 73-78, wherein the conjugate group is attached via the 2' position of a ribosyl sugar moiety at an internal position of the second modified oligonucleotide.

82. The oligomeric duplex of any of claims 73-81, wherein the conjugate group comprises a C22 alkyl, C20 alkyl, C16 alkyl, C10 alkyl, C21 alkyl, C19 alkyl, C18 alkyl, C17 alkyl, C15 alkyl, C14 alkyl, C13 alkyl, C12 alkyl, C11 alkyl, C9 alkyl, C8 alkyl, C7 alkyl, C6 alkyl, C5 alkyl, C22 alkenyl, C20 alkenyl, C16 alkenyl, C10 alkenyl, C21 alkenyl, C19 alkenyl, C18 alkenyl, C17 alkenyl, C15 alkenyl, C14 alkenyl, C13 alkenyl, C12 alkenyl, C11 alkenyl, C9 alkenyl, C8 alkenyl, C7 alkenyl, C6 alkenyl, or C5 alkenyl.

83. The oligomeric duplex of any of claims 73-82, wherein the conjugate group comprises a cell-targeting moiety.

84. The oligomeric duplex of any of claims 58-83, wherein the second modified oligonucleotide comprises a terminal group.

85. The oligomeric duplex of claim 84, wherein the terminal group is an abasic sugar moiety.

86. An antisense agent comprising or consisting of an antisense compound, wherein the antisense compound is the oligomeric compound of any of claims 1-49.

87. An antisense agent, wherein the antisense agent is the oligomeric duplex of any of claims 58-85.

88. The antisense agent of claim 86 or claim 87, wherein the antisense agent is:

i) an RNase H agent capable of reducing the amount of ATN1 nucleic acid through the activation of RNase H;

or

ii) an RNAi agent capable of reducing the amount of ATN1 nucleic acid through the activation of RISC/Ago2.

89. The antisense agent of any of claims 86-88, wherein the antisense agent comprises a conjugate group, and wherein the conjugate group comprises a cell-targeting moiety.

90. A pharmaceutical composition comprising an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, or an antisense agent of any of claims 86-89, and a pharmaceutically acceptable diluent.

91. The pharmaceutical composition of claim 90, wherein the pharmaceutically acceptable diluent is phosphate buffered saline (PBS) or artificial CSF (aCSF).

92. The pharmaceutical composition of claim 90 or claim 91, wherein the pharmaceutical composition consists essentially of the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, or the antisense agent, and aCSF.

93. The pharmaceutical composition of claim 90 or claim 91, wherein the pharmaceutical composition consists essentially of the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex 83, or the antisense agent, and PBS.

94. A method comprising administering to a subject an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, an antisense agent of any of claims 86-89, or a pharmaceutical composition of any of claims 90-93.

95. A method of treating a polyglutamine (polyQ) disease or disorder associated with ATN1 comprising administering to a subject having or at risk for developing the polyQ disease or disorder associated with ATN1 a therapeutically effective amount of an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, an antisense agent of any of claims 86-89, or a pharmaceutical composition of any of claims 90-93 and thereby treating the polyQ disease or disorder associated with ATN1.

96. The method of claim 95, wherein the polyQ disease or disorder associated with ATN1 is dentatorubral-pallidoluysian atrophy (DRPLA).

97. The method of claim 95 or 96, wherein at least one symptom or hallmark of the polyQ disease or disorder associated with ATN1 is ameliorated.

98. The method of claim 97, wherein the symptom or hallmark is seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

99. The method of claim 97 or claim 98, wherein administering the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition reduces or delays the onset or progression of seizure, ataxia, myoclonus, choreoathetosis, dementia, epilepsy, intellectual impairment, psychiatric symptoms, neuronal atrophy and dysfunction, action tremor, fetal cystic hygroma, atrophy of the dentate nucleus, dysarthria, dysdiadochokinesis, dysmetria, dyssynergia, hyperintensity of cerebral white matter on MRI, hyporeflexia, impaired proprioception, nystagmus, ophthalmoparesis, optic neuropathy, saccadic smooth pursuit, blepharospasm, memory impairment, oromandibular dystonia, or abnormal pyramidal sign.

100. The method of any of claims 94-99, wherein the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition is administered to the central nervous system or systemically.

101. The method of claim 100, wherein the oligomeric compound, the population of oligomeric compounds, the oligomeric duplex, the antisense agent, or the pharmaceutical composition is administered intrathecally.

102. The method of any of claims 94-101, wherein the subject is a human.

103. A method of reducing expression of ATN1 in a cell comprising contacting the cell with an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, an antisense agent of any of claims 86-89, or a pharmaceutical composition of any of claims 90-93.

104. The method of claim 103, wherein the cell is a brain cell.

105. The method of claim 103 or claim 104, wherein the cell is a human cell.

106. Use of an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, an antisense agent of any of claims 86-89, or a pharmaceutical composition of any of claims 90-93 for treating a polyglutamine (polyQ) disease or disorder associated with ATN1.

107. Use of an oligomeric compound of any of claims 1-49, a population of oligomeric compounds of any of claims 50-57, an oligomeric duplex of any of claims 58-85, an antisense agent of any of claims 86-89, or a pharmaceutical composition of any of claims 90-93 in the manufacture of a medicament for treating a polyglutamine (polyQ) disease or disorder associated with ATN1.

108. The use of claim 106 or claim 107, wherein the polyQ disease or disorder associated with ATN1 is dentatorubral-pallidoluysian atrophy (DRPLA).