COMPOUNDS AND METHODS FOR MODULATING ATXN1

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 BIOL0355WOSEQ_ST25.txt, created on April 26, 2021, which is 1.32 MB in size. The information in the electronic format of the sequence listing is incorporated herein by reference in its entirety.

Field

Provided are compounds, methods, and pharmaceutical compositions for reducing the amount or activity of ATXN1 RNA in a cell or subject, and in certain instances reducing the amount of ATXN1 protein in a cell or subject. Such compounds, methods, and pharmaceutical compositions are useful to ameliorate at least one symptom or hallmark of a neurodegenerative disease. Such symptoms and hallmarks include gait and limb ataxia, cognitive impairments, difficulty with speaking and swallowing, atrophy of the cerebellum and brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and brainstem detected via magnetic resonance spectroscopy (MRS), and death within 10-15 years of symptom onset. Such neurodegenerative diseases include Spinocerebellar ataxia type 1.

Background

Spinocerebellar ataxia type 1 (SCA1) is a progressive and fatal neurodegenerative disorder that affects 1-2/100,000 individuals worldwide. SCA1 is caused by an expanded CAG repeat in the coding region of gene encoding Ataxin-1, ATXN1. Accumulation of mutant Ataxin-1 protein leads to the degeneration of Purkinje cells and brainstem nuclei. Symptoms and hallmarks of SCA1 include gait and limb ataxia, cognitive impairments, difficulty with speaking and swallowing, atrophy of the cerebellum and brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and brainstem detected via magnetic resonance spectroscopy (MRS), and death within 10-15 years of symptom onset (see, e.g., Ju, H., Kokubu, H., and Lim, J., *Mol. Neurobiol.* 50:866-874, 2014; Ortiz, J. P., Orr, H. T., in Polyglutamine Disorders, Nóbrega, C. and Almeida, L., eds., *Advances in Exp. Med. And Biol.,* 1049: 135-145, 2018).

There are no specific therapies for SCA1, with current treatments being limited to supportive treatments for individual symptoms.

Currently there is a lack of acceptable options for treating neurodegenerative diseases such as SCA1. It is therefore an object herein to provide compounds, methods, and pharmaceutical compositions for the treatment of such diseases.

Summary of the Invention

Provided herein are compounds, methods and pharmaceutical compositions for reducing the amount or activity of ATXN1 RNA, and in certain embodiments reducing the expression of ATXN1 protein in a cell or subject. In certain embodiments, the subject has a neurodegenerative disease. In certain embodiments, the subject has Spinocerebellar ataxia type 1 (SCA1). In certain embodiments, compounds useful for reducing the amount or activity of ATXN1 RNA are oligomeric compounds. In certain embodiments, compounds useful for reducing the amount or activity of ATXN1

RNA are modified oligonucleotides. In certain embodiments, compounds useful for decreasing expression of ATXN1 protein are oligomeric compounds. In certain embodiments, compounds useful for decreasing expression of ATXN1 protein are modified oligonucleotides.

Also provided are methods useful for ameliorating at least one symptom or hallmark of a neurodegenerative disease. In certain embodiments, the neurodegenerative disease is Spinocerebellar ataxia type 1. In certain embodiments, the symptom or hallmark includes gait and limb ataxia, cognitive impairments, difficulty with speaking and swallowing, atrophy of the cerebellum and brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and brainstem detected via magnetic resonance spectroscopy (MRS), and death within 10-15 years of symptom onset.

Detailed Description of the Invention

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

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

Definitions

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

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

DEFINITIONS

As used herein, "2'-deoxynucleoside" means a nucleoside comprising a 2'-H(H) deoxyfuranosyl 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 may comprise a modified nucleobase or may comprise an RNA nucleobase (uracil).

As used herein, "2'-MOE" means a 2'-$OCH_2CH_2OCH_3$ group in place of the 2'-OH group of a furanosyl sugar moiety. A "2'-MOE sugar moiety" means a sugar moiety with a 2'-$OCH_2CH_2OCH_3$ group in place of the 2'-OH group

of a furanosyl sugar moiety. Unless otherwise indicated, a 2'-MOE sugar moiety is in the β-D-ribosyl configuration. "MOE" means O-methoxyethyl.

As used herein, "2'-MOE nucleoside" means a nucleoside comprising a 2'-MOE sugar moiety.

As used herein, "2'-OMe" means a 2'-OCH_3 group in place of the 2'-OH group of a furanosyl sugar moiety. A"2'-O-methyl sugar moiety" or "2'-OMe sugar moiety" means a sugar moiety with a 2'-OCH_3 group in place of the 2'-OH group of a furanosyl sugar moiety. Unless otherwise indicated, a 2'-OMe sugar moiety is in the β-D-ribosyl configuration.

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

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

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

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

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

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

As used herein, "ameliorate" in reference to a treatment means improvement in at least one symptom relative to the same symptom in the absence of the treatment. In certain embodiments, amelioration is the reduction in the severity or frequency of a symptom or the delayed onset or slowing of progression in the severity or frequency of a symptom. In certain embodiments, the symptom or hallmark is gait and limb ataxia, cognitive impairments, difficulty with speaking and swallowing, atrophy of the cerebellum and brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and brainstem detected via magnetic resonance spectroscopy (MRS), and death within 10-15 years of symptom onset.

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

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

As used herein, "cleavable moiety" means a bond or group of atoms that is cleaved under physiological conditions, for example, inside a cell, an animal, or a human.

As used herein, "complementary" in reference to an oligonucleotide means that at least 70% of the nucleobases of the oligonucleotide or one or more 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-methyl cytosine (mC) and guanine (G). Complementary oligonucleotides and/or target 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 portion thereof, means that the oligonucleotide, or a portion thereof, is complementary to another oligonucleotide or target 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, "conjugate group" means a group of atoms that is directly or indirectly attached to an oligonucleotide. Conjugate groups include a conjugate moiety and a conjugate linker that attaches the conjugate moiety to the oligonucleotide.

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

As used herein, "conjugate moiety" means a group of atoms that is attached to an oligonucleotide via a conjugate linker.

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

As used herein, "cEt" means a 4' to 2' bridge in place of the 2'OH-group of a ribosyl sugar moiety, wherein the bridge has the formula of 4'-CH(CH_3)-O-2', and wherein the methyl group of the bridge is in the S configuration. A "cEt sugar moiety" is a bicyclic sugar moiety with a 4' to 2' bridge in place of the 2'OH-group of a ribosyl sugar moiety, wherein the bridge has the formula of 4'-CH(CH_3)-O-2', and wherein the methyl group of the bridge is in the S configuration. "cEt" means constrained ethyl.

As used herein, "cEt nucleoside" means a nucleoside comprising a cEt sugar moiety. As used herein, "chirally enriched population" means a plurality of molecules of identical molecular formula, wherein the number or percentage of molecules within the population that contain a particular stereochemical configuration at a particular chiral center is greater than the number or percentage of molecules expected to contain the same particular stereochemical configuration at the same particular chiral center within the population if the particular chiral center were stereorandom. Chirally enriched populations of molecules having multiple chiral centers within each molecule may contain one or more stereorandom chiral centers. In certain embodiments, the molecules are modified oligonucleotides. In certain embodiments, the molecules are compounds comprising modified oligonucleotides.

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

As used herein, "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'-susbstituted 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, "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." 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 compound-mediated reduction of the amount or activity of the target nucleic acid.

As used herein, "hybridization" means the pairing or annealing of complementary oligonucleotides and/or nucleic acids. While not limited to a particular mechanism, the most common mechanism of hybridization involves hydrogen bonding, which may be Watson-Crick, Hoogsteen or reversed Hoogsteen hydrogen bonding, between complementary nucleobases.

As used herein, "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" is a modified internucleoside linkage in which one of the non-bridging oxygen atoms of a phosphodiester internucleoside linkage is replaced with a sulfur atom.

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

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

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

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

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-methyl cytosine" is a modified nucleobase. A universal base is a modified nucleobase that can pair with any one of the five unmodified nucleobases. As used herein, "nucleobase sequence" means the order of

contiguous nucleobases in a target nucleic acid or oligonucleotide independent of any sugar or internucleoside linkage modification.

As used herein, “nucleoside” means a compound or a 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 compound" means an oligonucleotide and optionally one or more additional features, such as a conjugate group or terminal group. An oligomeric compound may be paired with a second oligomeric compound that is complementary to the first oligomeric compound or may be unpaired. A “singled-stranded oligomeric compound” is an unpaired oligomeric compound. The term “oligomeric duplex” means a duplex formed by two oligomeric compounds having complementary nucleobase sequences. Each oligomeric compound of an oligomeric duplex may be referred to as a “duplexed oligomeric compound.”

As used herein, "oligonucleotide" means a strand of linked nucleosides connected via internucleoside linkages, wherein each nucleoside and internucleoside linkage may be modified or unmodified. Unless otherwise indicated, oligonucleotides consist of 8-50 linked nucleosides. As used herein, “modified oligonucleotide” means an oligonucleotide, wherein at least one nucleoside or internucleoside linkage is modified. As used herein, “unmodified oligonucleotide” means an oligonucleotide that does not comprise any nucleoside modifications or internucleoside modifications.

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

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

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

As used herein, “prodrug” means a therapeutic agent in a form outside the body that is converted to a different form within a subject or cells thereof. Typically, conversion of a prodrug within the subject 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.

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

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

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

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

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

As used herein, "standard *in vivo* assay" means the assay described in Example 6 and reasonable variations thereof.

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

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

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

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

As used herein, "symptom or hallmark" means any physical feature or test result that indicates the existence or extent of a disease or disorder. In certain embodiments, a symptom is apparent to a subject or to a medical professional examining or testing said subject. In certain embodiments, a hallmark is apparent upon invasive diagnostic testing, including, but not limited to, post-mortem tests. In certain embodiments, a hallmark is apparent on a brain MRI scan.

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

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

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

As used herein, “therapeutically effective amount” means an amount of a pharmaceutical agent that provides a therapeutic benefit to a subject. For example, a therapeutically effective amount improves a symptom or hallmark 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 30 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 90% complementary to an equal length portion of an ATXN1 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 30 linked nucleosides and having a nucleobase sequence comprising at least 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 22-3624 or 3655.

Embodiment 3. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 12, 13, 14, 15, 16, or 17 contiguous nucleobases of any of SEQ ID NOs: 3625-3654 or 3656-3669.

Embodiment 4. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 contiguous nucleobases complementary to:

an equal length portion of nucleobases 5472-5552 of SEQ ID NO: 1;
an equal length portion of nucleobases 5906-6005 of SEQ ID NO: 1;
an equal length portion of nucleobases 7868-7911 of SEQ ID NO: 1;
an equal length portion of nucleobases 8481-8514 of SEQ ID NO: 1; or
an equal length portion of nucleobases 446679-446706 of SEQ ID NO: 2.

Embodiment 5. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 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, or at least 17 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 196, 274, 352, 430, 508, 2578, 2655, 2732, 2809, 2886, 2963, 3121, 3122, 3190, 3191, 3192, 3262, 3330, 3331, 3332, 3401, 3402, 3575, 3577, 3620, 3624, 3638-3640, 3653-3655, 3662, 3665, 3669;
SEQ ID Nos: 42, 120, 198, 276, 509, 587, 2502, 2579, 2656, 2733, 2810, 2887, 2964, 3585, 3588-3590, 3615, 3618, 3622, 3657, 3660, 3661, 3663, 3664, 3666-3668;
SEQ ID Nos: 48, 126, 2044, 2121;
SEQ ID Nos: 128, 206, 284, 1045, 1122, 1199, and 1276; or
SEQ ID Nos: 2475, 2552, 2629, 2706, 2783, 3627-3630, 3644.

Embodiment 6. The oligomeric compound of any of embodiments 1-5, wherein the modified oligonucleotide has a nucleobase sequence that is at least 80%, 85%, 90%, 95%, or 100% complementary to the nucleobase sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 when measured across the entire nucleobase sequence of the modified oligonucleotide.

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 modified oligonucleotide comprises at least one modified nucleoside comprising a modified sugar moiety.

Embodiment 9. The oligomeric compound of embodiment 8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety.

Embodiment 10. The oligomeric compound of embodiment 9, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a bicyclic sugar moiety having a 2'-4' bridge, wherein the 2'-4' bridge is selected from –O-CH_2-; and –O-$CH(CH_3)$-.

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 or 2'-OMe modified sugar moiety.

Embodiment 13. The oligomeric compound of any of embodiments 7-8, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate.

Embodiment 14. The oligomeric compound of embodiment 13, wherein the modified oligonucleotide comprises at least one modified nucleoside comprising a sugar surrogate selected from morpholino and PNA.

Embodiment 15. The oligomeric compound of any of embodiments 1-8 or 11-14, wherein the modified oligonucleotide does not comprise a bicyclic sugar moiety.

Embodiment 16. The oligomeric compound of any of embodiments 1-15, wherein the modified oligonucleotide is a gapmer.

Embodiment 17. The oligomeric compound of any of embodiments 1-16, wherein the modified oligonucleotide has a sugar motif comprising:

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'-deoxyfuranosyl sugar moiety.

Embodiment 18. The oligomeric compound of embodiment 17, wherein the modified oligonucleotide has a sugar motif comprising:

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

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

a 3'-region consisting of 4 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the central region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 19. The oligomeric compound of embodiment 17, wherein the modified oligonucleotide has a sugar motif comprising:

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

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

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

each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the central region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 20. The oligomeric compound of embodiment 17, wherein the modified oligonucleotide has

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

a central region consisting of 8 linked central region nucleosides; and

a 3'-region consisting of 4 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a is a 2'-MOE nucleoside, and each of the central region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 21. The oligomeric compound of embodiment 17, wherein the modified oligonucleotide has

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

a central region consisting of 8 linked central region nucleosides; and

a 3'-region consisting of 4 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides comprises a 2'-MOE sugar moiety, each of the 3'-region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside, and each of the central region nucleosides comprises a 2'-β-D-deoxynucleoside.

Embodiment 22. The oligomeric compound of any of embodiments 1-16, wherein the modified oligonucleotide has a sugar motif comprising:

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 the central region has the following formula:

(Nd)(Nx)(Nd)n

wherein Nx is a 2'-OMe nucleoside and each Nd is a 2'-β-D-deoxynucleoside;

and n is from 6 to 8.

Embodiment 23. The oligomeric compound of any of embodiments 1-16, wherein the modified oligonucleotide has a sugar motif comprising:

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

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

a 3'-region consisting of 4 linked 3'-region nucleosides; wherein

each of the 5'-region nucleosides and each of the 3'-region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside,

and the central region has the following formula:

(Nd)(Nx)(Nd)n

wherein Nx is a 2'-OMe nucleoside and each Nd is a 2'-β-D-deoxynucleoside;

and n is 7.

Embodiment 24. The oligomeric compound of any of embodiments 1-23, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

Embodiment 25. The oligomeric compound of embodiment 24, wherein each internucleoside linkage of the modified oligonucleotide is a modified internucleoside linkage.

Embodiment 26. The oligomeric compound of embodiment 24 or 25 wherein the modified internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 27. The oligomeric compound of embodiment 24 or 26 wherein the modified oligonucleotide comprises at least one phosphodiester internucleoside linkage.

Embodiment 28. The oligomeric compound of any of embodiments 24, 26, or 27, wherein each internucleoside linkage is independently selected from a phosphodiester internucleoside linkage or a phosphorothioate internucleoside linkage.

Embodiment 29. The oligomeric compound of embodiments 1-24 or 26-28, wherein the modified oligonucleotide has an internucleoside linkage motif selected from among: sooossssssssssssooss, sssossssssssssssosss, sssossssssssoss, or sooooossssssssssoss; wherein,

s = a phosphorothioate internucleoside linkage and o = a phosphodiester internucleoside linkage.

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

Embodiment 31. The oligomeric compound of embodiment 30, wherein the modified nucleobase is a 5-methyl cytosine.

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, 16-18, 14-20, 15-17, 15-25, 16-20, or 17-20 linked nucleosides.

Embodiment 33. The oligomeric compound of any of embodiments 1-2, 4-19, 22 or 24-31, wherein the modified oligonucleotide consists of 18-22 or 18-20 linked nucleosides.

Embodiment 34. The oligomeric compound of any of embodiments 1-17 or 20-32, wherein the modified oligonucleotide consists of 17 linked nucleosides.

Embodiment 35. The oligomeric compound of any of embodiments 1-2, 4-19, 22 or 24-31, wherein the modified oligonucleotide consists of 20 linked nucleosides.

Embodiment 36. The oligomeric compound of any of embodiments 1-35, consisting of the modified oligonucleotide.

Embodiment 37. The oligomeric compound of any of embodiments 1-35, comprising a conjugate group comprising a conjugate moiety and a conjugate linker.

Embodiment 38. The oligomeric compound of embodiment 37, wherein the conjugate linker consists of a single bond.

Embodiment 39. The oligomeric compound of embodiment 37, wherein the conjugate linker is cleavable.

Embodiment 40. The oligomeric compound of embodiment 37, wherein the conjugate linker comprises 1-3 linker-nucleosides.

Embodiment 41. The oligomeric compound of any of embodiments 37-40, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

Embodiment 42. The oligomeric compound of any of embodiments 37-40, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 43. The oligomeric compound of any of embodiments 1-35 or 37-42, comprising a terminal group.

Embodiment 44. The oligomeric compound of any of embodiments 1-43 wherein the oligomeric compound is a singled-stranded oligomeric compound.

Embodiment 45. The oligomeric compound of any of embodiments 1-39 or 41-42, wherein the oligomeric compound does not comprise linker-nucleosides.

Embodiment 46. An oligomeric duplex comprising an oligomeric compound of any of embodiments 1-43 or 45.

Embodiment 47. An antisense compound comprising or consisting of an oligomeric compound of any of embodiments 1-45 or an oligomeric duplex of embodiment 46.

Embodiment 48. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 1-45 or an oligomeric duplex of embodiment 46 and a pharmaceutically acceptable carrier or diluent.

Embodiment 49. The pharmaceutical composition of embodiment 48, wherein the pharmaceutically acceptable diluent is artificial cerebral spinal fluid.

Embodiment 50. The pharmaceutical composition of embodiment 49, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebral spinal fluid.

Embodiment 51. A method comprising administering to a subject a pharmaceutical composition of any of embodiments 48-50.

Embodiment 52. A method of treating a disease associated with ATXN1 comprising administering to an individual having or at risk for developing a disease associated with ATXN1 a therapeutically effective amount of a pharmaceutical composition according to any of embodiments 48-50; and thereby treating the disease associated with ATXN1.

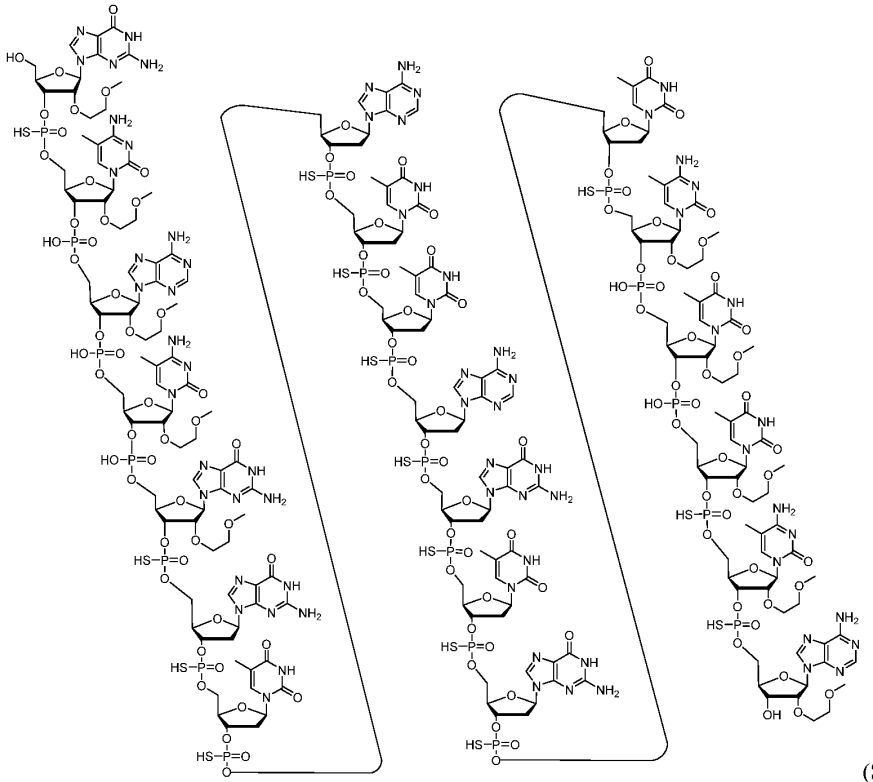
Embodiment 53. The method of embodiment 52, wherein the ATXN1-associated disease is Spinocerebellar ataxia type 1.

Embodiment 54. The method of any of embodiments 51-52, wherein at least one symptom or hallmark of the ATXN1-associated disease is ameliorated.

Embodiment 55. The method of embodiment 54, wherein the symptom or hallmark is gait or limb ataxia, cognitive impairments, difficulty with speaking or swallowing, atrophy of the cerebellum and/or brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and/or brainstem detected via magnetic resonance spectroscopy (MRS), or death within 10-15 years of symptom onset.

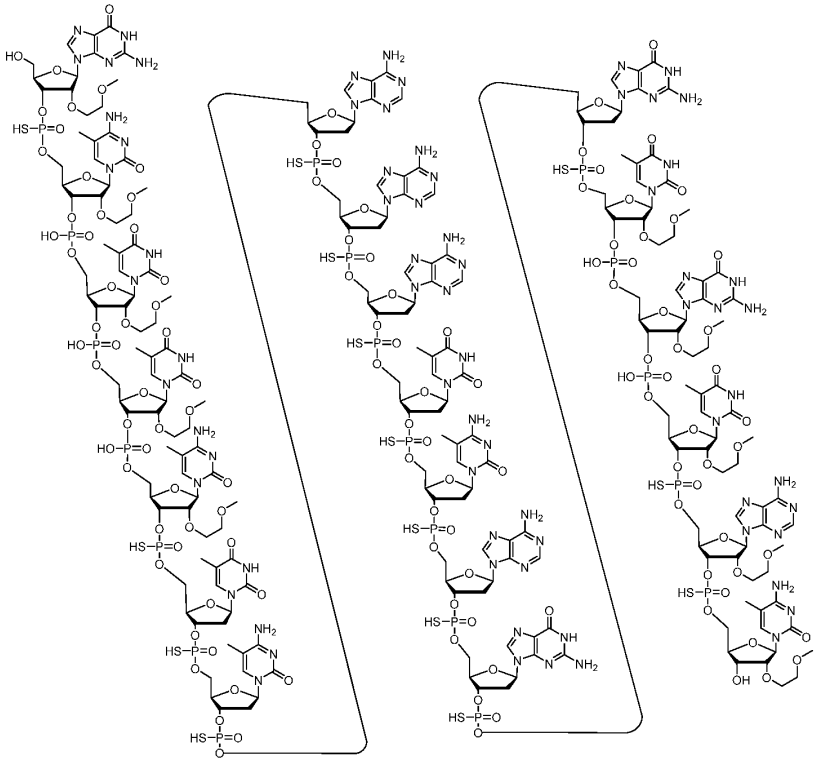
Embodiment 56. The method of any of embodiments 51-53, wherein ATXN1 levels in the individual are reduced.

Embodiment 57. A modified oligonucleotide according to the following chemical structure:



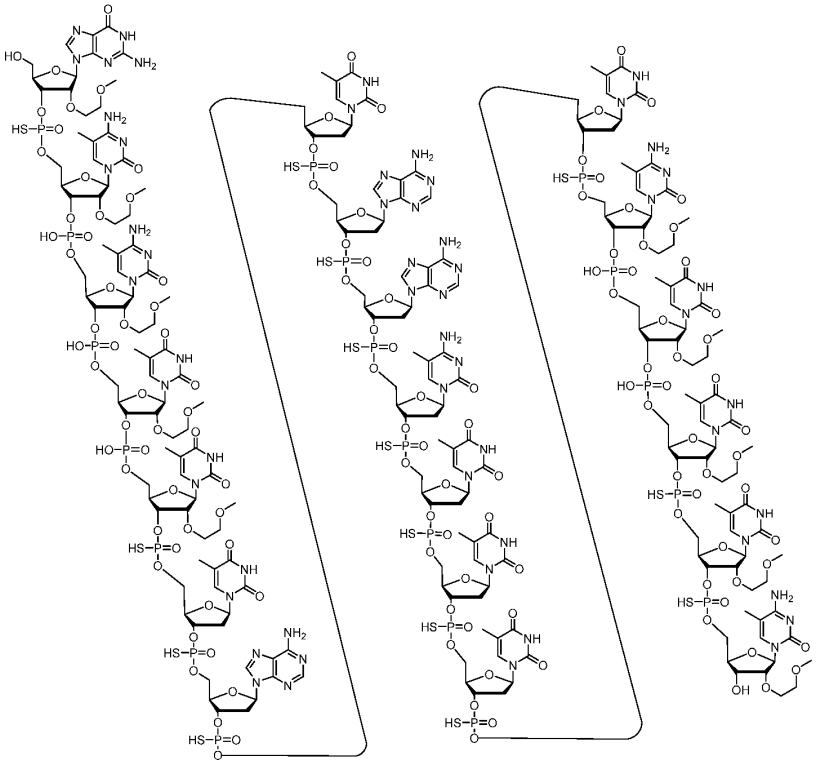
(SEQ ID NO: 126), or a salt thereof.

Embodiment 58. A modified oligonucleotide according to the following chemical structure:



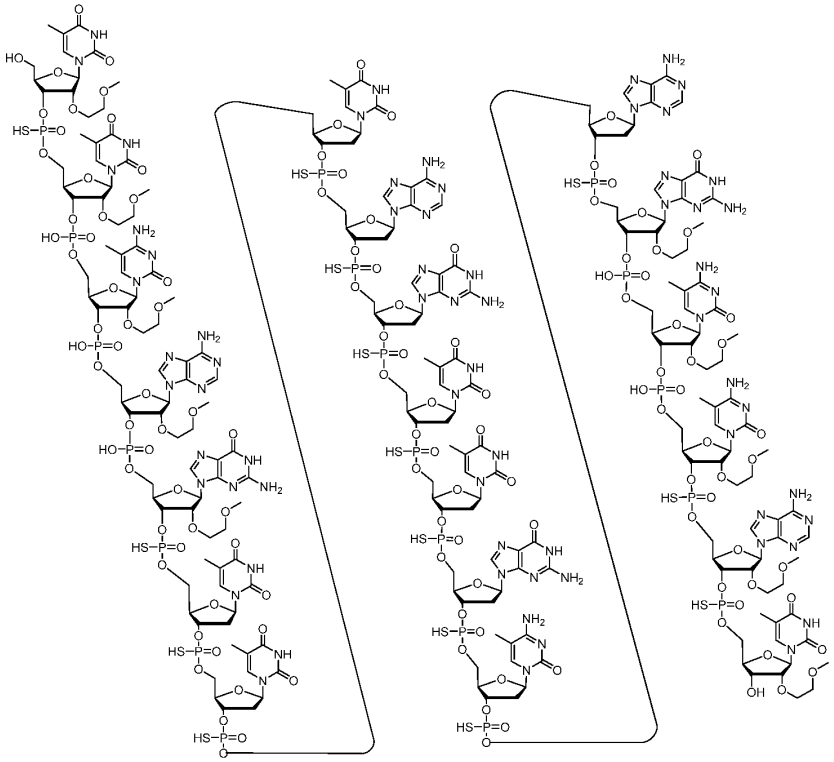
(SEQ ID NO: 1045), or a salt thereof.

Embodiment 59. A modified oligonucleotide according to the following chemical structure:



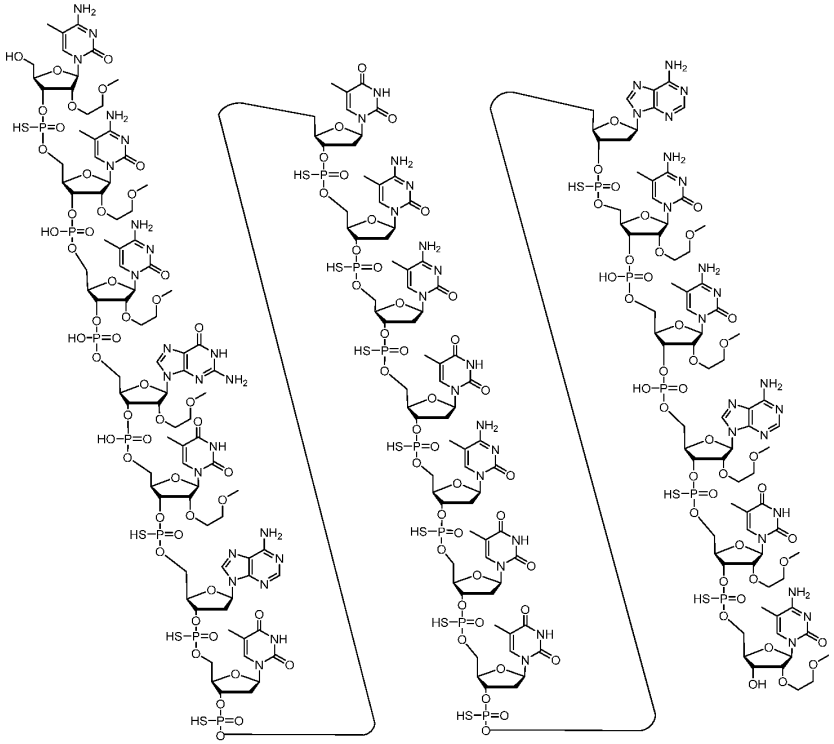
(SEQ ID NO: 2552), or a salt thereof.

Embodiment 60. A modified oligonucleotide according to the following chemical structure:



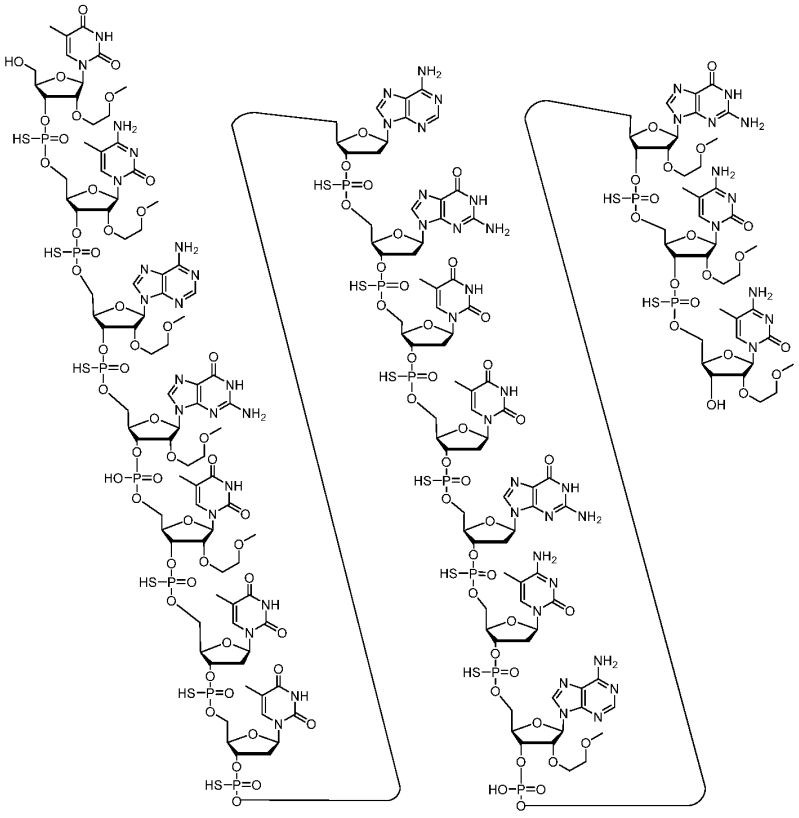
(SEQ ID NO: 3190), or a salt thereof.

Embodiment 61. A modified oligonucleotide according to the following chemical structure:



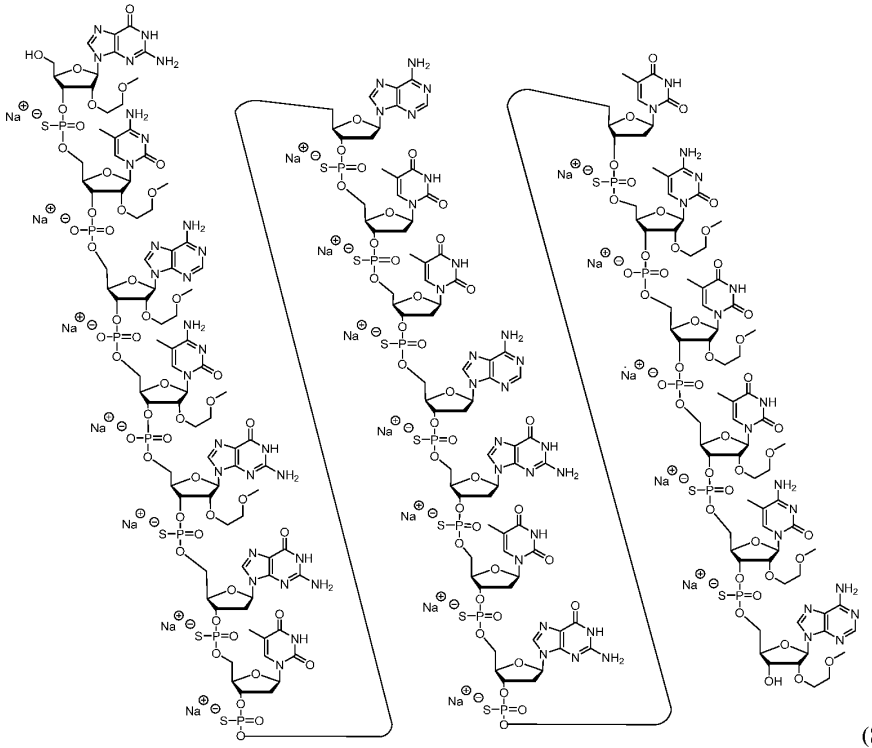
(SEQ ID NO: 3590), or a salt thereof.

Embodiment 62. A modified oligonucleotide according to the following chemical structure:



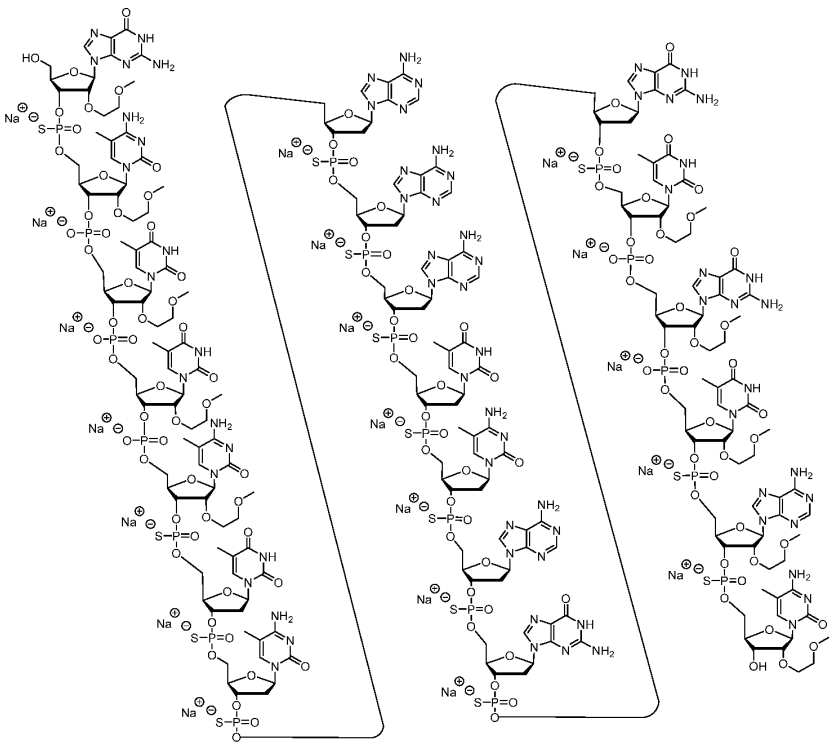
(SEQ ID NO: 3638), or a salt thereof.

Embodiment 63. A modified oligonucleotide according to the following chemical structure:



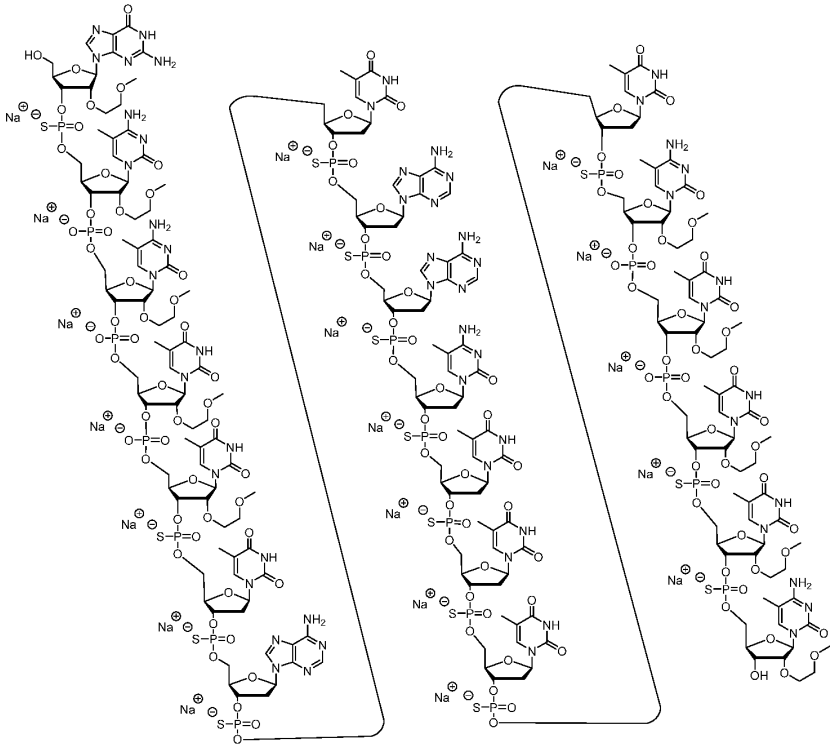
(SEQ ID NO: 126).

Embodiment 64. A modified oligonucleotide according to the following chemical structure:



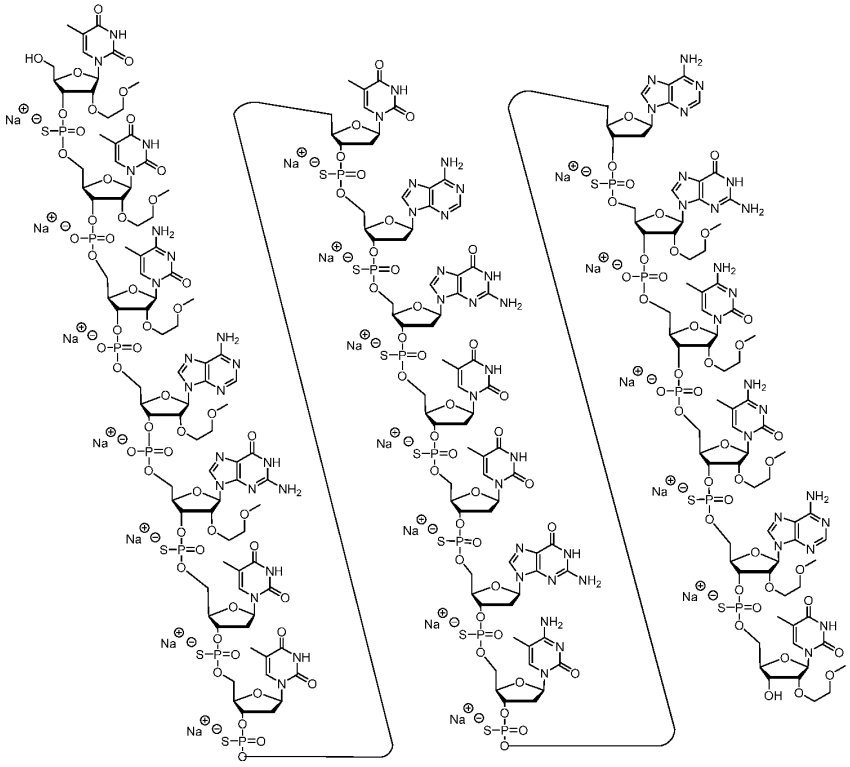
(SEQ ID NO: 1045).

Embodiment 65. A modified oligonucleotide according to the following chemical structure:



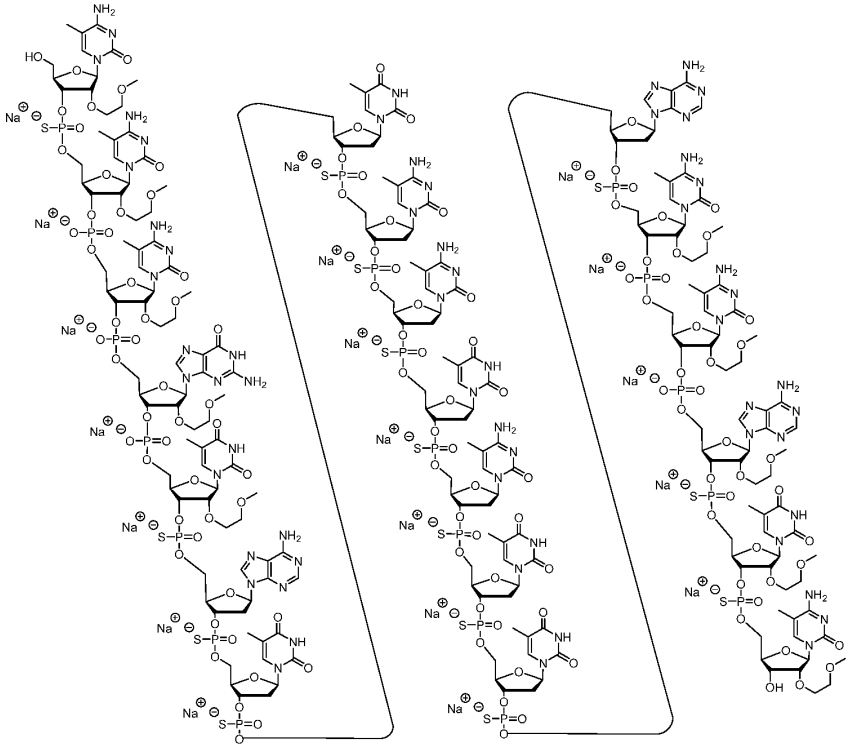
(SEQ ID NO: 2552).

Embodiment 66. A modified oligonucleotide according to the following chemical structure:



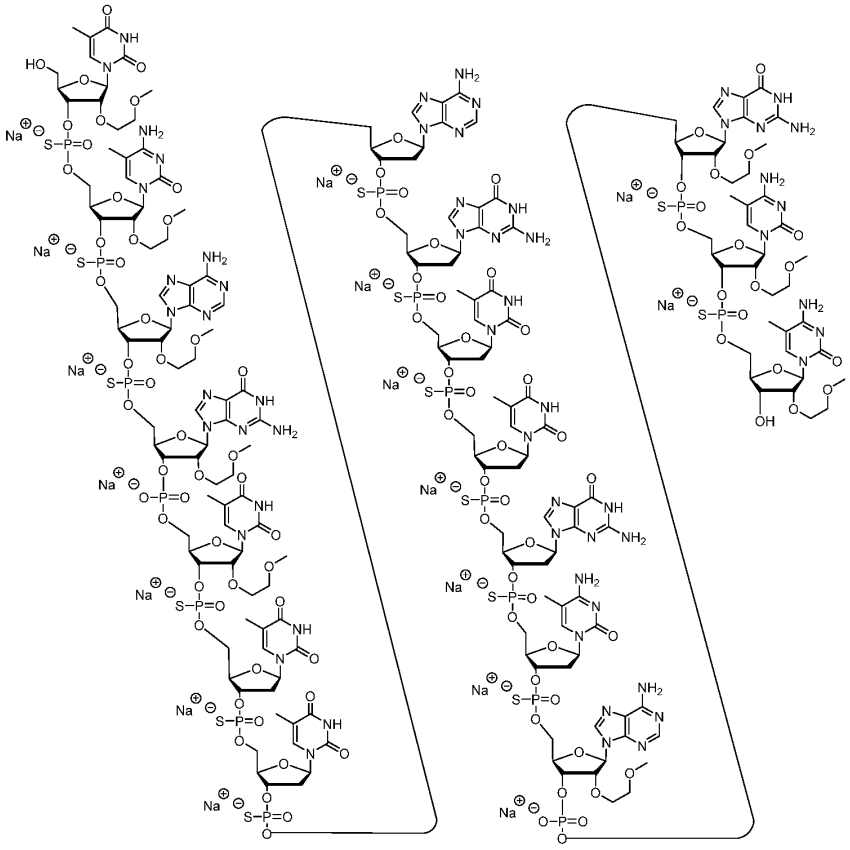
(SEQ ID NO: 3190).

Embodiment 67. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3590).

Embodiment 68. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3638).

Embodiment 69. The modified oligonucleotide of embodiment 57-62, which is a sodium salt or a potassium salt.

Embodiment 70. A compound comprising a modified oligonucleotide according to the following chemical notation:

Ges ^{m}Ceo Aeo ^{m}Ceo Ges Gds Tds Ads Tds Tds Ads Gds Tds Gds Tds ^{m}Ceo Teo Tes ^{m}Ces Ae (SEQ ID NO: 126), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 71. A compound comprising a modified oligonucleotide according to the following chemical notation:

Ges ^{m}Ceo Teo Teo ^{m}Ces Tds ^{m}Cds Ads Ads Ads Tds ^{m}Cds Ads Gds Gds Teo Geo Tes Aes mCe (SEQ ID NO: 1045), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
d = a 2'-β-D deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and
o = a phosphodiester internucleoside linkage.

Embodiment 72. A compound comprising a modified oligonucleotide according to the following chemical notation: Ges ^{m}Ceo ^{m}Ceo Teo Tes Tds Ads Tds Ads Ads ^{m}Cds Tds Tds Tds Tds ^{m}Ceo Teo Tes Tes ^{m}Ce (SEQ ID NO: 2552), wherein,

A = an adenine nucleobase,
^{m}C = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
d = a 2'-β-D deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and
o = a phosphodiester internucleoside linkage.

Embodiment 73. A compound comprising a modified oligonucleotide according to the following chemical notation: Tes Teo ^{m}Ceo Aeo Ges Tds Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Ads Geo ^{m}Ceo ^{m}Ces Aes Te (SEQ ID NO: 3190), wherein,

A = an adenine nucleobase,
^{m}C = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
d = a 2'-β-D deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and
o = a phosphodiester internucleoside linkage.

Embodiment 74. A compound comprising a modified oligonucleotide according to the following chemical notation: ^{m}Ces ^{m}Ceo ^{m}Ceo Geo Tes Ads Tds Tds ^{m}Cds ^{m}Cds Tds ^{m}Cds Tds Tds Ads ^{m}Ceo ^{m}Ceo Aes Tes ^{m}Ce (SEQ ID NO: 3590), wherein,

A = an adenine nucleobase,
^{m}C = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
d = a 2'-β-D deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 75. A compound comprising a modified oligonucleotide according to the following chemical notation: Tes ^{m}Ces Aes Geo Tes Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Aeo Ges ^{m}Ces ^{m}Ce (SEQ ID NO: 3638), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 76. The compound of any of embodiments 73-78, comprising the modified oligonucleotide covalently linked to a conjugate group.

Embodiment 77. A chirally enriched population of modified oligonucleotides of any of embodiments 57-68, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

Embodiment 78. The chirally enriched population of embodiment 77, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the *(Sp)* or *(Rp)* configuration.

Embodiment 79. The chirally enriched population of embodiment 77, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

Embodiment 80. The chirally enriched population of embodiment 77, 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 81. The chirally enriched population of embodiment 77 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 82. A population of modified oligonucleotides of any of embodiments 57-68, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

Embodiment 83. A pharmaceutical composition comprising the population of modified oligonucleotides of any of embodiments 77-82 and a pharmaceutically acceptable diluent or carrier.

Embodiment 84. A pharmaceutical composition of any of embodiments 62-75, and a pharmaceutically acceptable diluent or carrier.

Embodiment 85. The pharmaceutical composition of embodiment 84, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid or phosphate-buffered saline.

Embodiment 86. The pharmaceutical composition of embodiment 85, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebrospinal fluid or phosphate-buffered saline.

Embodiment 87. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion of an ATXN1 nucleic acid, and wherein the modified oligonucleotide comprises at least one modification selected from a modified sugar moiety and a modified internucleoside linkage.

Embodiment 88. The oligomeric compound of embodiment 87, wherein the ATXN1 nucleic acid has the nucleobase sequence of any of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

Embodiment 89. The oligomeric compound of embodiment 87 or embodiment 88, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases:

an equal length portion of nucleobases 5472-5552 of SEQ ID NO: 1;
an equal length portion of nucleobases 5906-6005 of SEQ ID NO: 1;
an equal length portion of nucleobases 7868-7911 of SEQ ID NO: 1;
an equal length portion of nucleobases 8481-8514 of SEQ ID NO: 1; or
an equal length portion of nucleobases 446679-446706 of SEQ ID NO: 2.

Embodiment 90. The oligomeric compound of any of embodiments 87-89, wherein the nucleobase sequence of the modified oligonucleotide is at least 80% complementary to an equal length portion within nucleobases:

an equal length portion of nucleobases 5489-5508 of SEQ ID NO: 1;
an equal length portion of nucleobases 5491-5507 of SEQ ID NO: 1;
an equal length portion of nucleobases 5912-5931 of SEQ ID NO: 1;
an equal length portion of nucleobases 7892-7911 of SEQ ID NO: 1;
an equal length portion of nucleobases 8481-8500 of SEQ ID NO: 1; or
an equal length portion of nucleobases 446680-446699 of SEQ ID NO: 2.

Embodiment 91. The oligomeric compound of any of embodiments 87-90, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length portion of the ATXN1 nucleic acid.

Embodiment 92. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides, wherein the modified oligonucleotide has a nucleobase sequence comprising at least 12, 13, 14, 15, 16, 17, 18, 19, or 20 contiguous nucleobases of any of SEQ ID NOs: 22-3624 or 3655.

Embodiment 93. An oligomeric compound comprising a modified oligonucleotide consisting of 12 to 30 linked nucleosides, wherein the modified oligonucleotide has a nucleobase sequence comprising at least 12, 13, 14, 15, 16, or 17 contiguous nucleobases of any of SEQ ID NOs: 3625-3654 or 3656-3669.

Embodiment 94. The oligomeric compound of embodiment 92 or 93, wherein the modified oligonucleotide has a nucleobase sequence comprising the nucleobase sequence of any of SEQ ID NO: 22-3669.

Embodiment 95. The oligomeric compound of embodiment 94, wherein the modified oligonucleotide has a nucleobase sequence consisting of the nucleobase sequence of any of SEQ ID NO: 22-3669.

Embodiment 96. The oligomeric compound of any of embodiments 92-95, wherein the modified oligonucleotide has 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, or at least 17 contiguous nucleobases of a sequence selected from:

SEQ ID NOs: 196, 274, 352, 430, 508, 2578, 2655, 2732, 2809, 2886, 2963, 3121, 3122, 3190, 3191,

3192, 3262, 3330, 3331, 3332, 3401, 3402, 3575, 3577, 3620, 3624, 3638-3640, 3653-3655, 3662, 3665, 3669;

SEQ ID Nos: 42, 120, 198, 276, 509, 587, 2502, 2579, 2656, 2733, 2810, 2887, 2964, 3585, 3588-3590, 3615, 3618, 3622, 3657, 3660, 3661, 3663, 3664, 3666-3668;

SEQ ID Nos: 48, 126, 2044, 2121;

SEQ ID Nos: 128, 206, 284, 1045, 1122, 1199, and 1276; or

SEQ ID Nos: 2475, 2552, 2629, 2706, 2783, 3627-3630, 3644.

Embodiment 97. The oligomeric compound of any of embodiments 92-95, wherein the modified oligonucleotide has 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, or 17 contiguous nucleobases of any of the nucleobase sequences of SEQ ID NO: 3638.

Embodiment 98. The oligomeric compound of any of embodiments 92-95, wherein the modified oligonucleotide has 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 any of the nucleobase sequences of SEQ ID NO: 126, 1045, 2552, 3190, or 3590.

Embodiment 99. The oligomeric compound of embodiment 97 or 98, wherein the modified oligonucleotide consists of 17 to 30 linked nucleosides and has a nucleobase sequence comprising the nucleobase sequence of any of 126, 1045, 2552, 3190, 3590, or 3638.

Embodiment 100. The oligomeric compound of embodiment 99, wherein the modified oligonucleotide has a nucleobase sequence consisting of the nucleobase sequence of any one of 126, 1045, 2552, 3190, 3590, or 3638.

Embodiment 101. The oligomeric compound of any of embodiments 92-100, wherein the nucleobase sequence of the modified oligonucleotide is at least 85%, at least 90%, at least 95%, or 100% complementary to an equal length portion of the ATXN1 nucleic acid, wherein the ATXN1 nucleic acid has the nucleobase sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6.

Embodiment 102. The oligomeric compound of any of embodiments 87-101, wherein at least one nucleoside of the modified oligonucleotide comprises a modified sugar moiety.

Embodiment 103. The oligomeric compound of embodiment 102, wherein the modified sugar moiety comprises a bicyclic sugar moiety.

Embodiment 104. The oligomeric compound of embodiment 103, wherein the bicyclic sugar moiety comprises a 2'-4' bridge selected from –O-CH_2-; and –O-CH(CH_3)-.

Embodiment 105. The oligomeric compound of any of embodiments 102-104, wherein the modified nucleoside comprises a non-bicyclic modified sugar moiety.

Embodiment 106. The oligomeric compound of embodiment 105, wherein the non-bicyclic modified sugar moiety is a 2'-MOE sugar moiety or 2'-OMe modified sugar moiety.

Embodiment 107. The oligomeric compound of any of embodiments 102-106, wherein at least one nucleoside of the modified oligonucleotide comprises a sugar surrogate.

Embodiment 108. The oligomeric compound of embodiment 107, wherein the sugar surrogate is selected from morpholino and PNA.

Embodiment 109. The oligomeric compound of any of embodiments 87-102 or 105-108, wherein the modified oligonucleotide does not comprise a bicyclic sugar moiety.

Embodiment 110. The oligomeric compound of any of embodiments 87-109, wherein the modified oligonucleotide comprises at least one modified internucleoside linkage.

Embodiment 111. The oligomeric compound of embodiment 110, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 112. The oligomeric compound of embodiment 110 or 111, wherein each internucleoside linkage is a modified internucleoside linkage.

Embodiment 113. The oligomeric compound of embodiment 112, wherein each internucleoside linkage is a phosphorothioate internucleoside linkage.

Embodiment 114. The oligomeric compound of any of embodiments 110-111, wherein at least one internucleoside linkage of the modified oligonucleotide is a phosphodiester internucleoside linkage.

Embodiment 115. The oligomeric compound of any of embodiments 87-109, wherein each internucleoside linkage of the modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage.

Embodiment 116. The oligomeric compound of any of embodiments 87-115, wherein at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, or at least 18 internucleoside linkages of the modified oligonucleotide are phosphorothioate internucleoside linkages.

Embodiment 117. The oligomeric compound of embodiment 116, wherein the modified oligonucleotide has an internucleoside linkage motif selected from: sooossssssssssssooss, sssossssssssssssosss, sssossssssssoss, or sooooossssssssssoss; wherein,

s = a phosphorothioate internucleoside linkage and o = a phosphodiester internucleoside linkage.

Embodiment 118. The oligomeric compound of any of embodiments 87-117, wherein the modified oligonucleotide comprises a modified nucleobase.

Embodiment 119. The oligomeric compound of embodiment 118, wherein the modified nucleobase is a 5-methyl cytosine.

Embodiment 120. The oligomeric compound of any of embodiments 1-33, wherein the modified oligonucleotide comprises a deoxy region consisting of 5-12 contiguous 2'-deoxynucleosides.

Embodiment 121. The oligomeric compound of embodiment 120, wherein each nucleoside of the deoxy region is a 2'-β-D-deoxynucleoside.

Embodiment 122. The oligomeric compound of embodiment 120 or 121 wherein the deoxy region consists of 6, 7, 8, 9, 10, or 6-10 linked nucleosides.

Embodiment 123. The oligomeric compound of any of embodiments 120-122, wherein each nucleoside immediately adjacent to the deoxy region comprises a modified sugar moiety.

Embodiment 124. The oligomeric compound of any of embodiments 120-122, 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'external region consisting of 1-6 linked 3'-region nucleosides; wherein

the 3'-most nucleoside of the 5'-region comprises a modified sugar moiety; and

the 5'-most nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 125. The oligomeric compound of embodiment 124, wherein each nucleoside of the 3'-region comprises a modified sugar moiety.

Embodiment 126. The oligomeric compound of embodiment 124 or 125, wherein each nucleoside of the 5'-region comprises a modified sugar moiety.

Embodiment 127. The oligomeric compound of embodiment 120-126, wherein the modified oligonucleotide has
a 5'-region consisting of 1-6 linked nucleosides;
a deoxy region consisting of 6-10 linked nucleosides; and
a 3'-region consisting of 1-6 linked nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides comprises a modified sugar moiety.

Embodiment 128. The oligomeric compound of embodiment 127, wherein the modified oligonucleotide has
a 5'-region consisting of 6 linked nucleosides;
a deoxy region consisting of 10 linked nucleosides; and
a 3'-region consisting of 4 linked nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the deoxy region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 129. The oligomeric compound of embodiment 127, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked nucleosides;
a central region consisting of 10 linked nucleosides; and
a 3'-region consisting of 5 linked nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the deoxy region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 130. The oligomeric compound of embodiment 127, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked nucleosides;
a deoxy region consisting of 8 linked nucleosides; and
a 3'-region consisting of 4 linked nucleosides; wherein
each of the 5'-region nucleosides and each of the 3'-region nucleosides is a 2'-MOE nucleoside, and each of the deoxy region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 131. The oligomeric compound of embodiment 127, wherein the modified oligonucleotide has
a 5'-region consisting of 5 linked nucleosides;
a deoxy region consisting of 8 linked nucleosides; and
a 3'-region consisting of 4 linked nucleosides; wherein
each of the 5'-region nucleosides is a 2'-MOE nucleoside, each of the 3'-region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside, and each of the deoxy region nucleosides is a 2'-β-D-deoxynucleoside.

Embodiment 132. The oligomeric compound of any of embodiments 87-119, wherein the modified oligonucleotide has
a 5' region consisting of 3-7 linked nucleosides;
a deoxy region consisting of 6-8 linked nucleosides; and

a 3' region consisting of 3-6 linked nucleosides; wherein
each of the 3' region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside, and the 5' region has the following formula:
(Nk)n(Nd)(Nx)
wherein each Nk is a bicyclic nucleoside, Nx is a 2'-OMe nucleoside and Nd is a 2'-β-D-deoxynucleoside;
and n is from 1-5.

Embodiment 133. The oligomeric compound of any of embodiments 87-119, wherein the modified oligonucleotide has
a 5' region consisting of 7 linked nucleosides;
a deoxy region consisting of 6 linked nucleosides; and
a 3' region consisting of 4 linked nucleosides; wherein
each of the 3' region nucleosides is selected from a 2'-MOE nucleoside and a cEt nucleoside, and the 5' region has the following formula:
(Nk)n(Nd)(Nx)
wherein each Nk is a bicyclic nucleoside, Nx is a 2'-OMe nucleoside and Nd is a 2'-β-D-deoxynucleoside;
and n is from 5.

Embodiment 134. The oligomeric compound of any of embodiments 87-133, wherein the modified oligonucleotide consists of 12-30, 12-22, 12-20, 14-18, 16-18, 14-20, 15-17, 15-25, 16-20, or 17-20 linked nucleosides.

Embodiment 135. The oligomeric compound of any of embodiments 87-132, wherein the modified oligonucleotide consists of 18-22 or 18-20 linked nucleosides.

Embodiment 136. The oligomeric compound of any of embodiments 87-133, wherein the modified oligonucleotide consists of 17 linked nucleosides.

Embodiment 137. The oligomeric compound of any of embodiments 87-132, wherein the modified oligonucleotide consists of 20 linked nucleosides.

Embodiment 138. A compound comprising a modified oligonucleotide according to the following chemical notation:
Ges ^{m}Ceo Aeo ^{m}Ceo Ges Gds Tds Ads Tds Tds Ads Gds Tds Gds Tds ^{m}Ceo Teo Tes ^{m}Ces Ae (SEQ ID NO: 126), wherein,
A = an adenine nucleobase,
^{m}C = a 5-methyl cytosine nucleobase,
G = a guanine nucleobase,
T = a thymine nucleobase,
e = a 2'-MOE sugar moiety,
d = a 2'-β-D deoxyribosyl sugar moiety,
s = a phosphorothioate internucleoside linkage, and
o = a phosphodiester internucleoside linkage.

Embodiment 139. A compound comprising a modified oligonucleotide according to the following chemical

notation:

Ges ^{m}Ceo Teo Teo ^{m}Ces Tds ^{m}Cds Ads Ads Ads Tds ^{m}Cds Ads Gds Gds Teo Geo Tes Aes mCe (SEQ ID NO: 1045), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 140. A compound comprising a modified oligonucleotide according to the following chemical notation:

Ges ^{m}Ceo ^{m}Ceo Teo Tes Tds Ads Tds Ads Ads ^{m}Cds Tds Tds Tds Tds ^{m}Ceo Teo Tes Tes ^{m}Ce (SEQ ID NO: 2552), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 141. A compound comprising a modified oligonucleotide according to the following chemical notation:

Tes Teo ^{m}Ceo Aeo Ges Tds Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Ads Geo ^{m}Ceo ^{m}Ces Aes Te (SEQ ID NO: 3190), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 142. A compound comprising a modified oligonucleotide according to the following chemical notation:

^{m}Ces ^{m}Ceo ^{m}Ceo Geo Tes Ads Tds Tds ^{m}Cds ^{m}Cds Tds ^{m}Cds Tds Tds Ads ^{m}Ceo ^{m}Ceo Aes Tes ^{m}Ce (SEQ ID NO: 3590), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 143. A compound comprising a modified oligonucleotide according to the following chemical notation:

Tes ^{m}Ces Aes Geo Tes Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Aeo Ges ^{m}Ces ^{m}Ce (SEQ ID NO: 3638), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

Embodiment 144. The oligomeric compound of any of embodiments 87-143, consisting of the modified oligonucleotide.

Embodiment 145. The oligomeric compound of any of embodiments 87-144, comprising a conjugate group comprising a conjugate moiety and a conjugate linker.

Embodiment 146. The oligomeric compound of embodiment 145, wherein the conjugate linker consists of a single bond.

Embodiment 147. The oligomeric compound of embodiment 145, wherein the conjugate linker is cleavable.

Embodiment 148. The oligomeric compound of embodiment 145, wherein the conjugate linker comprises 1-3 linker nucleosides.

Embodiment 149. The oligomeric compound of any of embodiments 145-148, wherein the conjugate linker does not comprise any linker nucleosides.

Embodiment 150. The oligomeric compound of any of embodiments 145-148, wherein the conjugate group is attached to the modified oligonucleotide at the 5'-end of the modified oligonucleotide.

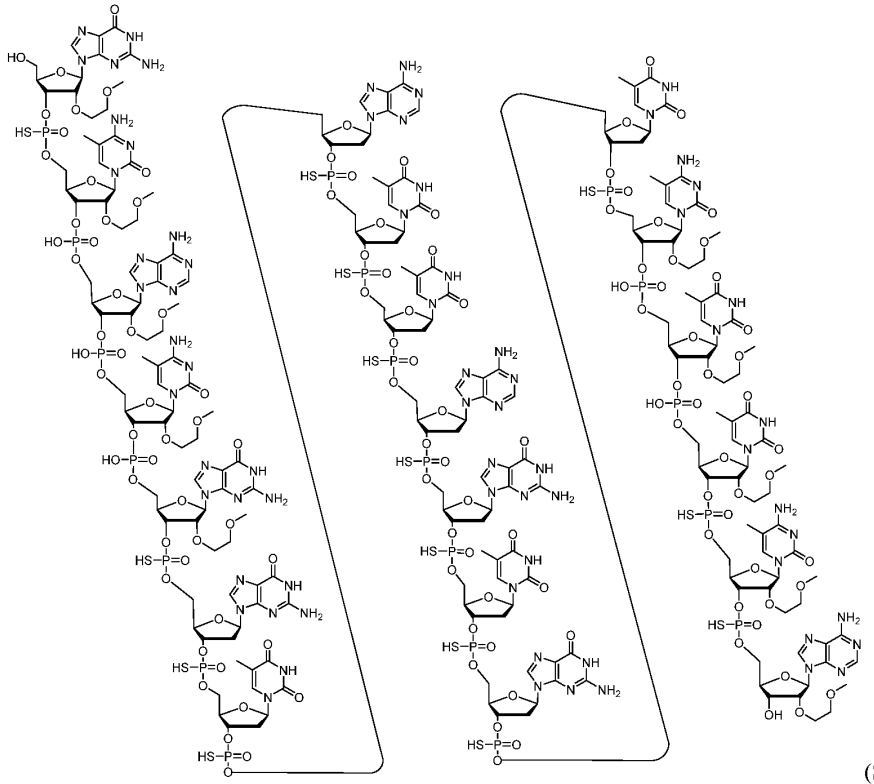
Embodiment 151. The oligomeric compound of any of embodiments 145-148, wherein the conjugate group is attached to the modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 152. The oligomeric compound of any of embodiments 87-143 or 146-148, comprising a terminal group.

Embodiment 153. The oligomeric compound of embodiment 152, wherein the terminal group is an abasic sugar moiety.

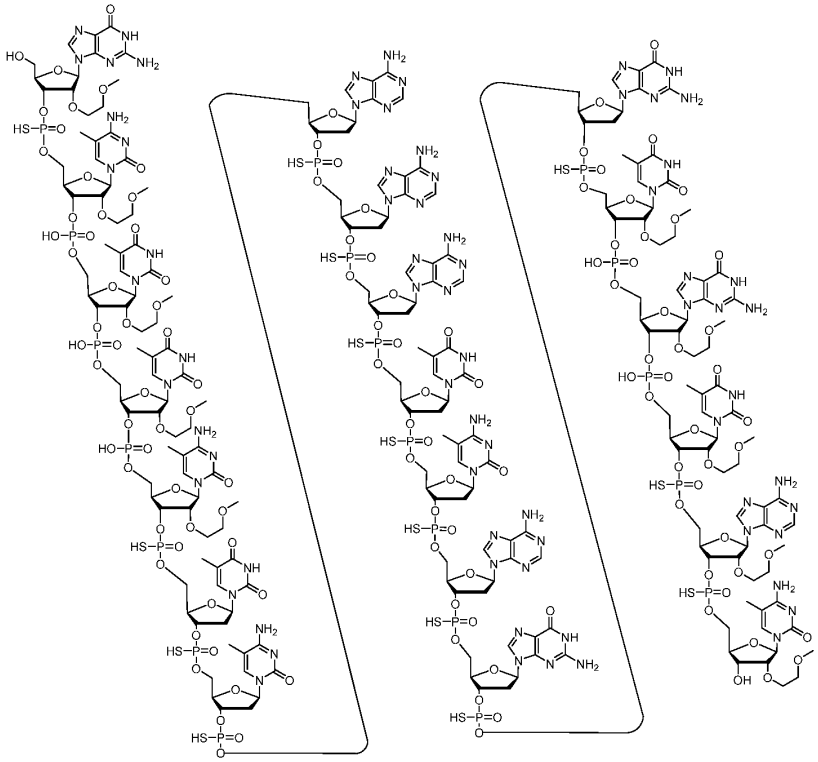
Embodiment 154. The oligomeric compound of any of embodiments 87-153 wherein the oligomeric compound is a singled-stranded oligomeric compound.

Embodiment 155. A modified oligonucleotide according to the following chemical structure:



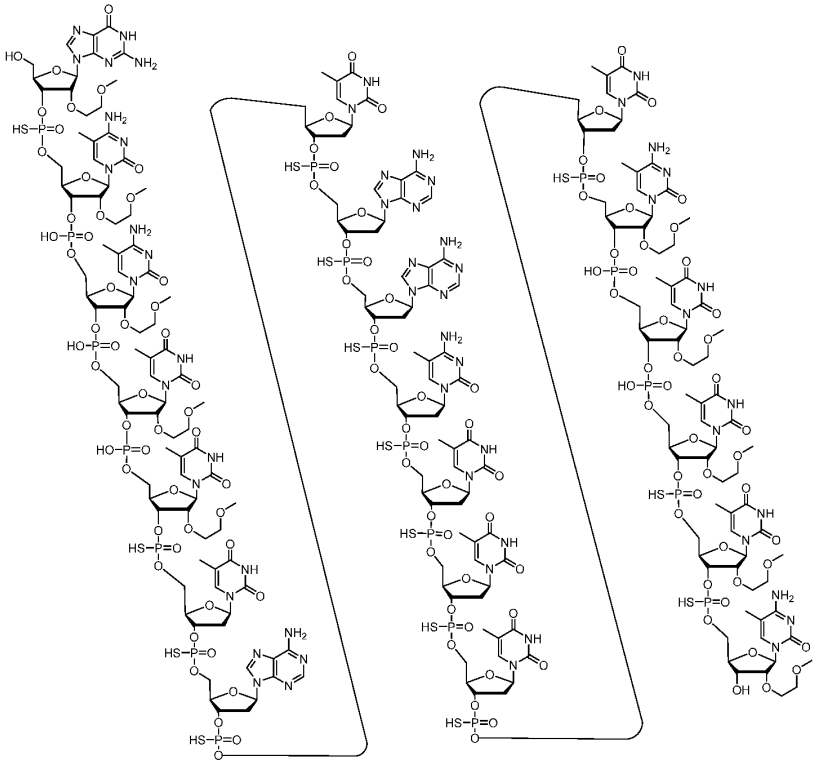
(SEQ ID NO: 126), or a salt thereof.

Embodiment 156. A modified oligonucleotide according to the following chemical structure:



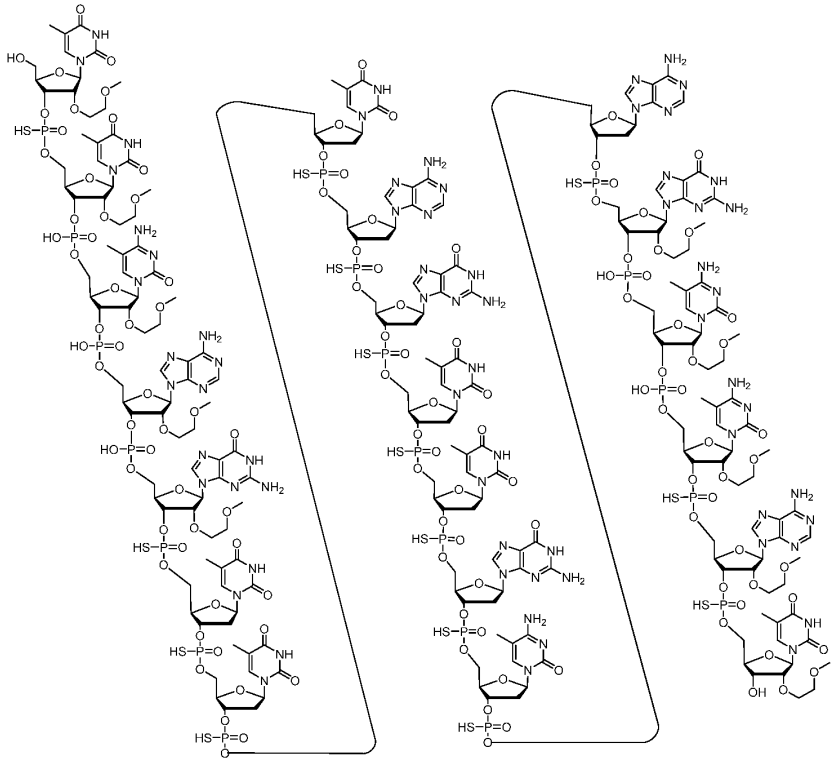
(SEQ ID NO: 1045), or a salt thereof.

Embodiment 157. A modified oligonucleotide according to the following chemical structure:



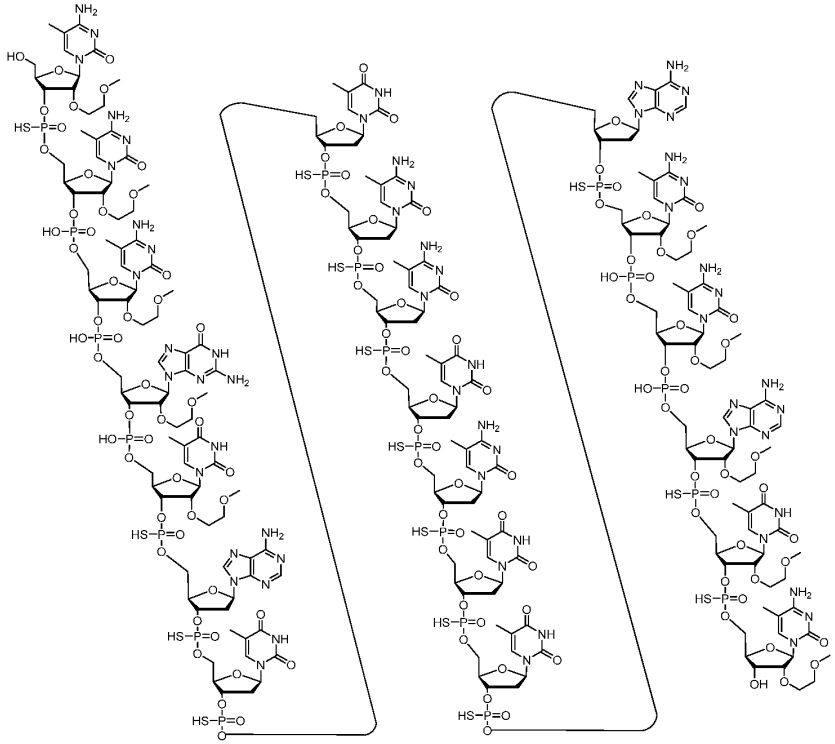
(SEQ ID NO: 2552), or a salt thereof.

Embodiment 158. A modified oligonucleotide according to the following chemical structure:



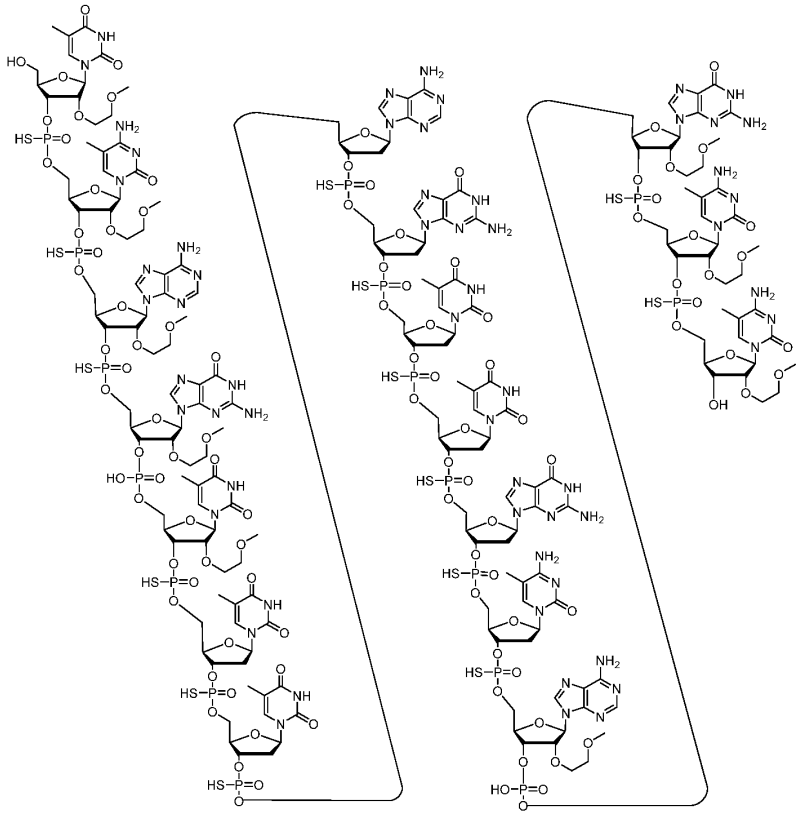
(SEQ ID NO: 3190), or a salt thereof.

Embodiment 159. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3590), or a salt thereof.

Embodiment 160. A modified oligonucleotide according to the following chemical structure:

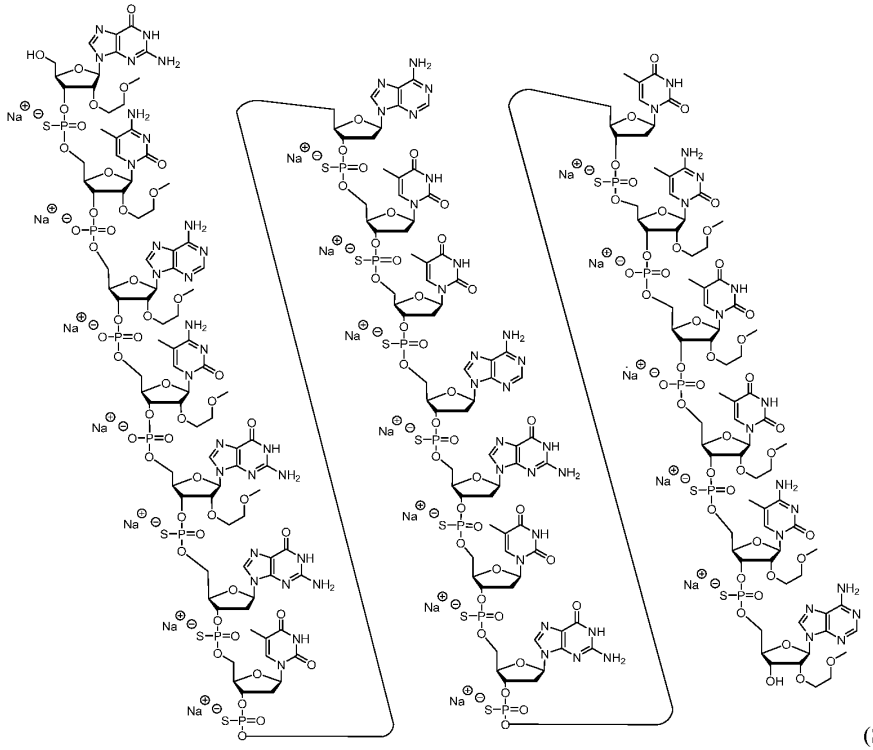


(SEQ ID NO: 3638),

or a salt thereof.

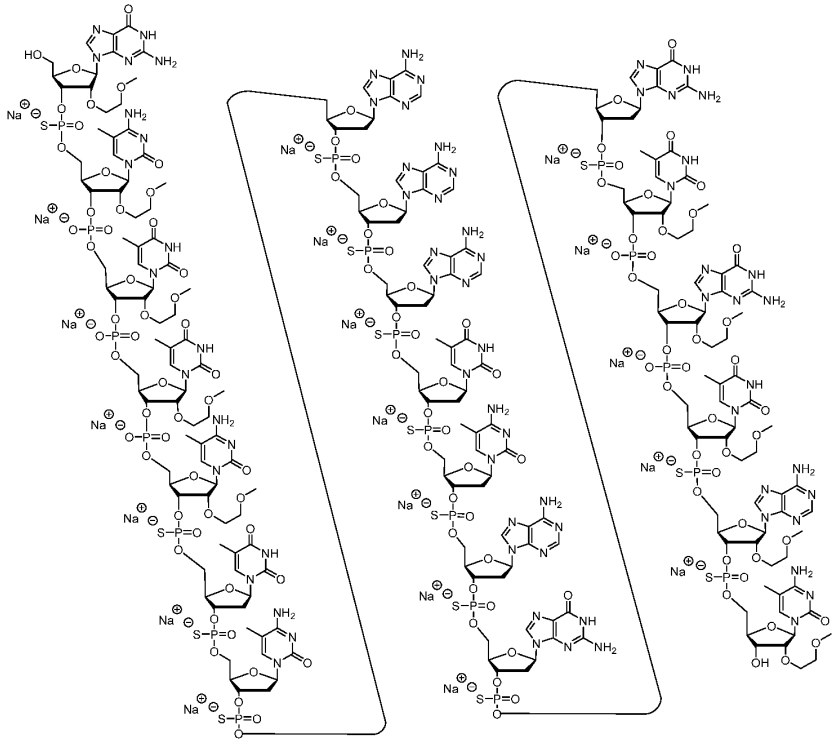
Embodiment 161. The modified oligonucleotide of any of embodiments 155-160, which is the sodium salt or the potassium salt.

Embodiment 162. A modified oligonucleotide according to the following chemical structure:



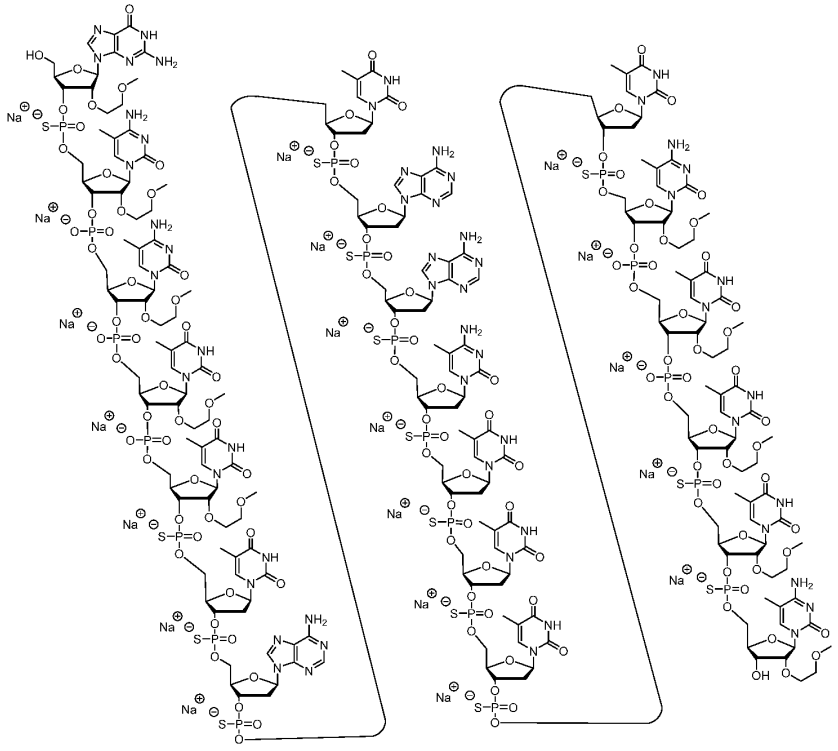
(SEQ ID NO: 126).

Embodiment 163. A modified oligonucleotide according to the following chemical structure:



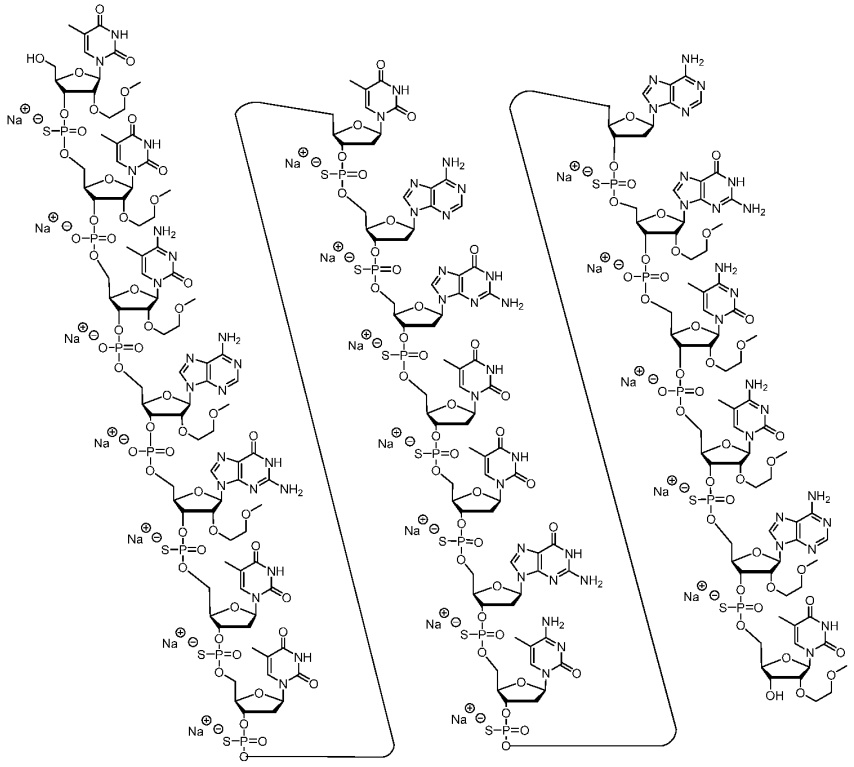
(SEQ ID NO: 1045).

Embodiment 164. A modified oligonucleotide according to the following chemical structure:



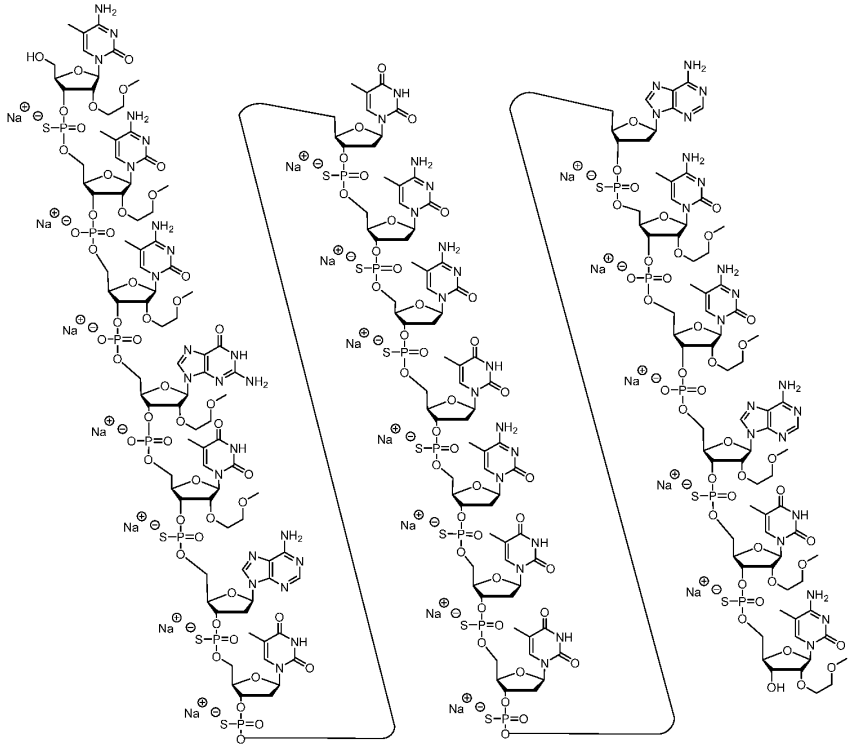
(SEQ ID NO: 2552).

Embodiment 165. A modified oligonucleotide according to the following chemical structure:



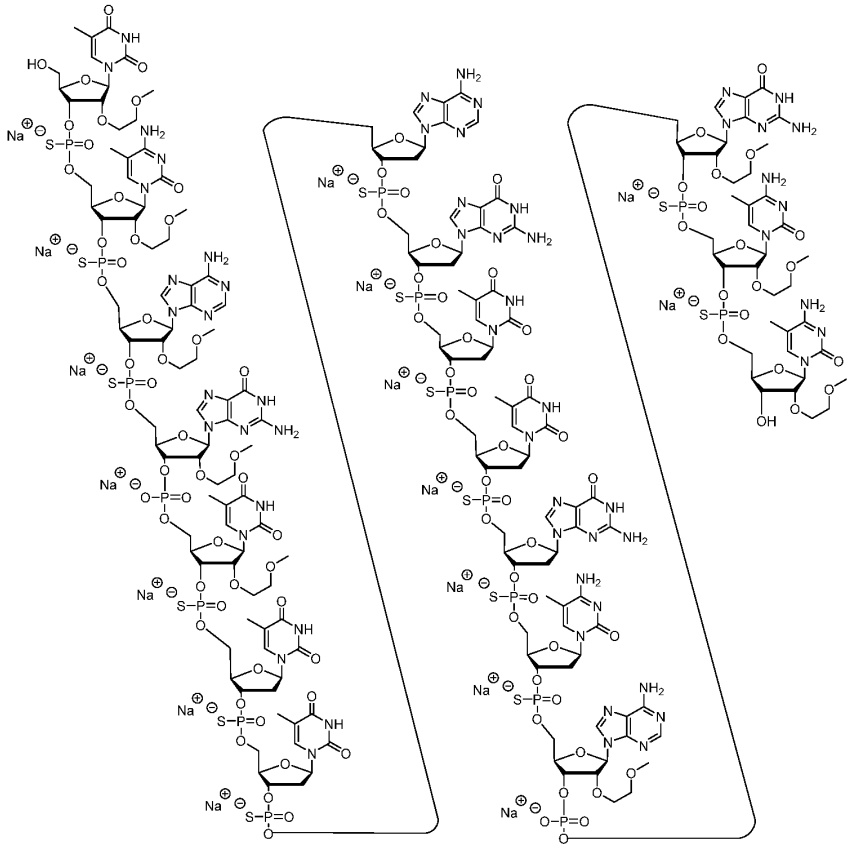
(SEQ ID NO: 3190).

Embodiment 166. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3590).

Embodiment 167. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3638).

Embodiment 168. A chirally enriched population of oligomeric compounds of any of embodiments 87-154 or modified oligonucleotide of embodiments 155-167, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having a particular stereochemical configuration.

Embodiment 169. The chirally enriched population of embodiment 168, wherein the population is enriched for modified oligonucleotides comprising at least one particular phosphorothioate internucleoside linkage having the *(Sp)* or *(Rp)* configuration.

Embodiment 170. The chirally enriched population of embodiment 169, wherein the population is enriched for modified oligonucleotides having a particular, independently selected stereochemical configuration at each phosphorothioate internucleoside linkage.

Embodiment 171. The chirally enriched population of embodiment 170, 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 172. The chirally enriched population of embodiment 171, 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 173. A population of oligomeric compounds comprising modified oligonucleotides of any of embodiments 87-154, or a population of modified oligonucleotides of embodiments 155-167, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotide are stereorandom.

Embodiment 174. 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 87-154.

Embodiment 175. The oligomeric duplex of embodiment 174, wherein the second oligomeric compound comprises a second modified oligonucleotide consisting of 12 to 30 linked nucleosides, and wherein the nucleobase sequence of the second modified oligonucleotide comprises a complementary region of at least 8 nucleobases that is at least 90% complementary to an equal length portion of the first modified oligonucleotide.

Embodiment 176. The oligomeric duplex of embodiment 174 or 175, wherein the modified oligonucleotide of the first oligomeric compound comprises a 5'-stabilized phosphate group.

Embodiment 177. The oligomeric duplex of embodiment 176, wherein the stabilized phosphate group comprises a cyclopropyl phosphonate or a vinyl phosphonate.

Embodiment 178. The oligomeric duplex of any of embodiments 174-177, wherein the modified oligonucleotide of the first oligomeric compound comprises a glycol nucleic acid (GNA) sugar surrogate.

Embodiment 179. The oligomeric duplex of any of embodiments 174-178, wherein the modified oligonucleotide of the first oligomeric compound comprises a 2'-NMA sugar moiety.

Embodiment 180. The oligomeric duplex of any of embodiments 174-179, wherein at least one nucleoside of the second modified oligonucleotide comprises a modified sugar moiety.

Embodiment 181. The oligomeric duplex of embodiment 180, wherein the modified sugar moiety of the second modified oligonucleotide comprises a bicyclic sugar moiety.

Embodiment 182. The oligomeric duplex of embodiment 181, wherein the bicyclic sugar moiety of the second modified oligonucleotide comprises a 2'-4' bridge selected from –O-CH_2-; and –O-$CH(CH_3)$-.

Embodiment 183. The oligomeric duplex of embodiment 182, wherein the modified sugar moiety of the second modified oligonucleotide comprises a non-bicyclic modified sugar moiety.

Embodiment 184. The oligomeric duplex of embodiment 183, wherein the non-bicyclic modified sugar moiety of the second modified oligonucleotide is a 2'-MOE sugar moiety, a 2'-F sugar moiety, or 2'-OMe sugar moiety.

Embodiment 185. The oligomeric duplex of any of embodiments 174-184, wherein at least one nucleoside of the second modified oligonucleotide comprises a sugar surrogate.

Embodiment 186. The oligomeric duplex of any of embodiments 174-185, wherein at least one internucleoside linkage of the second modified oligonucleotide is a modified internucleoside linkage.

Embodiment 187. The oligomeric duplex of embodiment 186, wherein at least one modified internucleoside linkage of the second modified oligonucleotide is a phosphorothioate internucleoside linkage.

Embodiment 188. The oligomeric duplex of any of embodiments 174-187, wherein at least one internucleoside linkage of the second modified oligonucleotide is a phosphodiester internucleoside linkage.

Embodiment 189. The oligomeric duplex of any of embodiments 174-188, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester or a phosphorothioate internucleoside linkage.

Embodiment 190. The oligomeric duplex of any of embodiments 174-189, wherein each internucleoside linkage of the second modified oligonucleotide is independently selected from a phosphodiester internucleoside linkage, a phosphorothioate internucleoside linkage, or a mesyl phosphoramidate internucleoside linkage.

Embodiment 191. The oligomeric duplex of any of embodiments 174-190, wherein the second modified oligonucleotide comprises at least one modified nucleobase.

Embodiment 192. The oligomeric duplex of embodiment 191, wherein the modified nucleobase of the second modified oligonucleotide is 5-methylcytosine.

Embodiment 193. The oligomeric duplex of any of embodiments 174-192, wherein the second modified oligonucleotide comprises a conjugate group.

Embodiment 194. The oligomeric duplex of embodiment 193, wherein the conjugate group comprises a conjugate linker and a conjugate moiety.

Embodiment 195. The oligomeric duplex of embodiment 193 or 194, wherein the conjugate group is attached to the second modified oligonucleotide at the 5'-end of the second modified oligonucleotide.

Embodiment 196. The oligomeric duplex of embodiment 193 or 194, wherein the conjugate group is attached to the second modified oligonucleotide at the 3'-end of the modified oligonucleotide.

Embodiment 197. The oligomeric duplex of any of embodiments 193-196, wherein the second modified oligonucleotide comprises a terminal group.

Embodiment 198. The oligomeric duplex of embodiment 197, wherein the terminal group is an abasic sugar moiety.

Embodiment 199. The oligomeric duplex of any of embodiments 174-198, wherein the second modified oligonucleotide consists of 10 to 25, 10 to 30, 10 to 50, 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, 20 to 50, 21 to 25, 21 to 30, 21 to 50, 22 to 25, 22 to 30, 22 to 50, 23 to 25, 23 to 30, or 23 to 50 linked nucleosides.

Embodiment 200. An antisense agent comprising an antisense compound, wherein the antisense compound is the oligomeric compound of any of embodiments 87-154 or the modified oligonucleotide of any of embodiments 155-167.

Embodiment 201. The antisense agent of embodiment 200, wherein the antisense agent is the oligomeric duplex of any of embodiments 174-199.

Embodiment 202. The antisense agent of embodiment 200 or 201, wherein the antisense agent is an RNase H agent capable of reducing the amount of ATXN1 nucleic acid through the activation of RNase H.

Embodiment 203. The antisense agent of any of embodiments 200-202, wherein the conjugate group comprises a cell-targeting moiety.

Embodiment 204. A pharmaceutical composition comprising an oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, an oligomeric duplex of any of embodiments 174-199, or an antisense agent of any of embodiments 200-203, and a pharmaceutically acceptable carrier or diluent.

Embodiment 205. The pharmaceutical composition of embodiment 204, wherein the pharmaceutically acceptable diluent is water, phosphate-buffered saline, or artificial cerebral spinal fluid.

Embodiment 206. The pharmaceutical composition of embodiment 205, wherein the pharmaceutical composition consists essentially of the modified oligonucleotide and artificial cerebral spinal fluid.

Embodiment 207. A method comprising administering to a subject the oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, the oligomeric duplex of any of embodiments 174-199, the antisense agent of any of embodiments 200-203, or the pharmaceutical composition of any of embodiments 204-206.

Embodiment 208. A method of treating a disease associated with ATXN1 comprising administering to a subject having a disease associated with ATXN1 a therapeutically effective amount of the oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, the oligomeric duplex of any of embodiments 174-199, the antisense agent of any of embodiments 200-203, or the pharmaceutical composition of any of embodiments 204-206; thereby treating the disease associated with ATXN1.

Embodiment 209. The method of embodiment 208, wherein the ATXN1-associated disease is Spinocerebellar ataxia type 1.

Embodiment 210. The method of any of embodiments 208-209, wherein at least one symptom or hallmark of the ATXN1-associated disease is ameliorated.

Embodiment 211. The method of embodiment 210, wherein the symptom or hallmark is gait or limb ataxia, cognitive impairments, difficulty with speaking or swallowing, atrophy of the cerebellum and/or brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and/or brainstem detected via magnetic resonance spectroscopy (MRS), or death within 10-15 years of symptom onset.

Embodiment 212. The method of any of embodiments 208-211, wherein ATXN1 levels in the subject are reduced.

Embodiment 213. A method of reducing expression of ATXN1 in a cell comprising contacting the cell with the oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, the oligomeric duplex of any of embodiments 174-199, the antisense agent of any of embodiments 200-203, or the pharmaceutical composition of any of embodiments 204-206.

Embodiment 214. The method of embodiment 213, wherein the cell is a CNS cell.

Embodiment 215. Use of the oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, the oligomeric duplex of any of embodiments 174-199, the antisense agent of any of embodiments 200-203, or the pharmaceutical composition of any of embodiments 204-206 for treating a disease associated with ATXN1.

Embodiment 216. Use of the oligomeric compound of any of embodiments 87-154, the modified oligonucleotide of any of embodiments 155-167, the population of any of embodiments 168-173, the oligomeric duplex of any of embodiments 174-199, the antisense agent of any of embodiments 200-203, or the pharmaceutical composition of any of embodiments 204-206 in the manufacture of a medicament for treating a disease associated with ATXN1.

Embodiment 217. The use of embodiment 215 or 216, wherein the disease associated with ATXN1 is Spinocerebellar ataxia type 1.

I. Certain Oligonucleotides

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

A. Certain Modified Nucleosides

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

1. Certain Sugar Moieties

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

In certain embodiments, modified sugar moieties are non-bicyclic modified sugar moieties comprising a furanosyl ring with one or more substituent groups none of which bridges two atoms of the furanosyl ring to form a bicyclic structure. Such non bridging substituents may be at any position of the furanosyl, including but not limited to substituents at the 2', 4', and/or 5' positions. In certain embodiments one or more non-bridging substituent of non-bicyclic modified sugar moieties is branched. Examples of 2'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to: 2'-F, 2'-OCH_3 ("OMe" or "O-methyl"), and 2'-$O(CH_2)_2OCH_3$ ("MOE" or "O-methoxyethyl"). In certain embodiments, 2'-substituent groups are selected from among: halo, allyl, amino, azido, SH, CN, OCN, CF_3, OCF_3, O-C_1-C_{10} alkoxy, O-C_1-C_{10} substituted alkoxy, O-C_1-C_{10} alkyl, O-C_1-C_{10} substituted alkyl, S-alkyl, N(R_m)-alkyl, O-alkenyl, S-alkenyl, N(R_m)-alkenyl, O-alkynyl, S-alkynyl, N(R_m)-alkynyl, O-alkylenyl-O-alkyl, alkynyl, alkaryl, aralkyl, O-alkaryl, O-aralkyl, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$ or $OCH_2C(=O)$-$N(R_m)(R_n)$, where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl, and the 2'-substituent groups described in Cook et al., U.S. 6,531,584; Cook et al., U.S. 5,859,221; and Cook et al., U.S. 6,005,087. Certain embodiments of these 2'-substituent groups can be further substituted with one or more substituent groups independently selected from among: hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro (NO_2), thiol, thioalkoxy, thioalkyl, halogen, alkyl, aryl, alkenyl and alkynyl. Examples of 4'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to alkoxy (*e.g.*, methoxy), alkyl, and those described in Manoharan et al., WO 2015/106128. Examples of 5'-substituent groups suitable for non-bicyclic modified sugar moieties include but are not limited to: 5-methyl (R or S), 5'-vinyl, and 5'-methoxy. In certain embodiments, non-bicyclic modified sugar moieties comprise more than one non-bridging sugar substituent, for example, 2'-F-5'-methyl sugar moieties and the modified sugar moieties and modified nucleosides described in Migawa et al., WO 2008/101157 and Rajeev et al., US2013/0203836.

In certain embodiments, a 2'-substituted non-bicyclic modified nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, NH_2, N_3, OCF_3, OCH_3, $O(CH_2)_3NH_2$, $CH_2CH{=}CH_2$, $OCH_2CH{=}CH_2$, $OCH_2CH_2OCH_3$, $O(CH_2)_2SCH_3$, $O(CH_2)_2ON(R_m)(R_n)$, $O(CH_2)_2O(CH_2)_2N(CH_3)_2$, and N-substituted

acetamide ($OCH_2C(=O)$-$N(R_m)(R_n)$), where each R_m and R_n is, independently, H, an amino protecting group, or substituted or unsubstituted C_1-C_{10} alkyl.

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

In certain embodiments, a 2'-substituted nucleoside comprises a sugar moiety comprising a non-bridging 2'-substituent group selected from: F, OCH_3, and $OCH_2CH_2OCH_3$.

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-deoxyribosyl 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-ribosyl isomeric configuration unless otherwise specified.

Certain modifed sugar moieties comprise a substituent that bridges two atoms of the furanosyl ring to form a second ring, resulting in a bicyclic sugar moiety. In certain such embodiments, the bicyclic sugar moiety comprises a bridge between the 4' and the 2' furanose ring atoms. Examples of such 4' to 2' bridging sugar substituents include but are not limited to: 4'-CH_2-2', 4'-$(CH_2)_2$-2', 4'-$(CH_2)_3$-2', 4'-CH_2-O-2' ("LNA"), 4'-CH_2-S-2', 4'-$(CH_2)_2$-O-2' ("ENA"), 4'-$CH(CH_3)$-O-2' (referred to as "constrained ethyl" or "cEt"), 4'-CH_2-O-CH_2-2', 4'-CH_2-N(R)-2', 4'-$CH(CH_2OCH_3)$-O-2' ("constrained MOE" or "cMOE") and analogs thereof (*see, e.g.,* Seth et al., U.S. 7,399,845, Bhat et al., U.S. 7,569,686, Swayze et al., U.S. 7,741,457, and Swayze et al., U.S. 8,022,193), 4'-$C(CH_3)(CH_3)$-O-2' and analogs thereof (*see, e.g.,*Seth et al., U.S. 8,278,283), 4'-CH_2-$N(OCH_3)$-2' and analogs thereof (*see, e.g.,* Prakash et al., U.S. 8,278,425), 4'-CH_2-O-$N(CH_3)$-2' (*see, e.g.,* Allerson et al., U.S. 7,696,345 and Allerson et al., U.S. 8,124,745), 4'-CH_2-$C(H)(CH_3)$-2' (*see, e.g.,* Zhou, *et al., J. Org. Chem.,*2009, *74*, 118-134), 4'-CH_2-$C(=CH_2)$-2' and analogs thereof (*see e.g.*, Seth et al., U.S. 8,278,426), 4'-$C(R_aR_b)$-N(R)-O-2', 4'-$C(R_aR_b)$-O-N(R)-2', 4'-CH_2-O-N(R)-2', and 4'-CH_2-N(R)-O-2', wherein each R, R_a, and R_b is, independently, H, a protecting group, or C_1-C_{12} alkyl (*see, e.g.* Imanishi et al., U.S. 7,427,672).

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

wherein:

x is 0, 1, or 2;

n is 1, 2, 3, or 4;

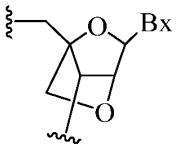
each R_a and R_b is, independently, H, a protecting group, hydroxyl, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, heterocycle radical, substituted heterocycle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

each J_1 and J_2 is, independently, H, C_1-C_{12} alkyl, substituted C_1-C_{12} alkyl, C_2-C_{12} alkenyl, substituted C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, substituted C_2-C_{12} alkynyl, C_5-C_{20} aryl, substituted C_5-C_{20} aryl, acyl (C(=O)-H), substituted

acyl, a heterocycle radical, a substituted heterocycle radical, C_1-C_{12} aminoalkyl, substituted C_1-C_{12} aminoalkyl, or a protecting group.

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

In certain embodiments, bicyclic sugar moieties and nucleosides incorporating such bicyclic sugar moieties are further defined by isomeric configuration. For example, an LNA nucleoside (described herein) may be in the α-L configuration or in the β-D configuration.



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



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

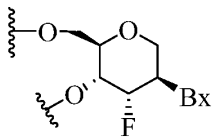
α-L-methyleneoxy (4'-CH_2-O-2') or α-L-LNA bicyclic nucleosides have been incorporated into oligonucleotides that showed antisense activity (Frieden et al., *Nucleic Acids Research,* 2003, *21*, 6365-6372). Herein, general descriptions of bicyclic nucleosides include both isomeric configurations. When the positions of specific bicyclic nucleosides (*e.g.*, LNA or cEt) are identified in exemplified embodiments herein, they are in the β-D configuration, unless otherwise specified.

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

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

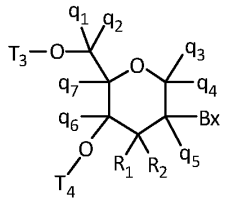
In certain embodiments, sugar surrogates comprise rings having other than 5 atoms. For example, in certain embodiments, a sugar surrogate comprises a six-membered tetrahydropyran ("THP"). Such tetrahydropyrans may be further modified or substituted. Nucleosides comprising such modified tetrahydropyrans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

hexitol nucleic acid ("HNA"), anitol nucleic acid ("ANA"), manitol nucleic acid ("MNA") (*see, e.g.,* Leumann, CJ. *Bioorg. & Med. Chem.* 2002, *10*, 841-854), fluoro HNA:



F-HNA

("F-HNA", *see e.g.* Swayze et al., U.S. 8,088,904; Swayze et al., U.S. 8,440,803; Swayze et al., U.S. 8,796,437; and Swayze et al., U.S. 9,005,906; F-HNA can also be referred to as a F-THP or 3'-fluoro tetrahydropyran), and nucleosides comprising additional modified THP compounds having the formula:



wherein, independently, for each of the modified THP nucleosides:

Bx is a nucleobase moiety;

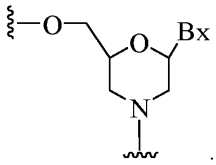
T_3 and T_4 are each, independently, an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide or one of T_3 and T_4 is an internucleoside linking group linking the modified THP nucleoside to the remainder of an oligonucleotide and the other of T_3 and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

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

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

In certain embodiments, modified THP nucleosides are provided wherein q_1, q_2, q_3, q_4, q_5, q_6 and q_7 are each H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is other than H. In certain embodiments, at least one of q_1, q_2, q_3, q_4, q_5, q_6 and q_7 is methyl. In certain embodiments, modified THP nucleosides are provided wherein one of R_1 and R_2 is F. In certain embodiments, R_1 is F and R_2 is H, in certain embodiments, R_1 is methoxy and R_2 is H, and in certain embodiments, R_1 is methoxyethoxy and R_2 is H.

In certain embodiments, sugar surrogates comprise rings having more than 5 atoms and more than one heteroatom. For example, nucleosides comprising morpholino sugar moieties and their use in oligonucleotides have been reported (*see, e.g.,* Braasch et al., Biochemistry, 2002, *41*, 4503-4510 and Summerton et al., U.S. 5,698,685; Summerton et al., U.S. 5,166,315; Summerton et al., U.S. 5,185,444; and Summerton et al., U.S. 5,034,506). As used here, the term "morpholino" means a sugar surrogate having the following structure:



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

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

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

2. Certain Modified Nucleobases

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

In certain embodiments, modified nucleobases are selected from: 5-substituted pyrimidines, 6-azapyrimidines, alkyl or alkynyl substituted pyrimidines, alkyl substituted purines, and N-2, N-6 and O-6 substituted purines. In certain embodiments, modified nucleobases are selected from: 2-aminopropyladenine, 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-N-methylguanine, 6-N-methyladenine, 2-propyladenine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-propynyl (-C≡C-CH_3) uracil, 5-propynylcytosine, 6-azouracil, 6-azocytosine, 6-azothymine, 5-ribosyluracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl, 8-aza and other 8-substituted purines, 5-halo, particularly 5-bromo, 5-trifluoromethyl, 5-halouracil, and 5-halocytosine, 7-methylguanine, 7-methyladenine, 2-F-adenine, 2-aminoadenine, 7-deazaguanine, 7-deazaadenine, 3-deazaguanine, 3-deazaadenine, 6-N-benzoyladenine, 2-N-isobutyrylguanine, 4-N-benzoylcytosine, 4-N-benzoyluracil, 5-methyl 4-N-benzoylcytosine, 5-methyl 4-N-benzoyluracil, universal bases, hydrophobic bases, promiscuous bases, size-expanded bases, and fluorinated bases. Further modified nucleobases include tricyclic pyrimidines, such as 1,3-diazaphenoxazine-2-one, 1,3-diazaphenothiazine-2-one and 9-(2-aminoethoxy)-1,3-diazaphenoxazine-2-one (G-clamp). Modified nucleobases may also include those in which the purine or pyrimidine base is replaced with other heterocycles, for example 7-deaza-adenine, 7-deazaguanosine, 2-aminopyridine and 2-pyridone. Further nucleobases include those disclosed in Merigan et al., U.S. 3,687,808, those disclosed in *The Concise Encyclopedia Of Polymer Science And Engineering*, Kroschwitz, J.I., Ed., John Wiley & Sons, 1990, 858-859; Englisch *et al.*, *Angewandte Chemie*, International Edition, 1991, *30*, 613; Sanghvi, Y.S., Chapter 15, *Antisense Research and Applications*, Crooke, S.T. and Lebleu, B., Eds., CRC Press, 1993, 273-288; and those disclosed in Chapters 6 and 15, *Antisense Drug Technology*, Crooke S.T., Ed., CRC Press, 2008, 163-166 and 442-443.

Publications that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include without limitation, Manoharan et al., US2003/0158403; Manoharan et al., US2003/0175906; Dinh et al., U.S. 4,845,205; Spielvogel et al., U.S. 5,130,302; Rogers et al., U.S. 5,134,066;

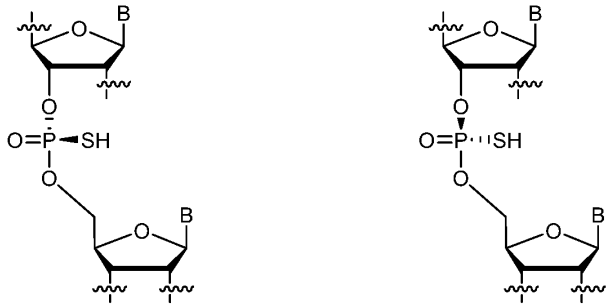
Bischofberger et al., U.S. 5,175,273; Urdea et al., U.S. 5,367,066; Benner et al., U.S. 5,432,272; Matteucci et al., U.S. 5,434,257; Gmeiner et al., U.S. 5,457,187; Cook et al., U.S. 5,459,255; Froehler et al., U.S. 5,484,908; Matteucci et al., U.S. 5,502,177; Hawkins et al., U.S. 5,525,711; Haralambidis et al., U.S. 5,552,540; Cook et al., U.S. 5,587,469; Froehler et al., U.S. 5,594,121; Switzer et al., U.S. 5,596,091; Cook et al., U.S. 5,614,617; Froehler et al., U.S. 5,645,985; Cook et al., U.S. 5,681,941; Cook et al., U.S. 5,811,534; Cook et al., U.S. 5,750,692; Cook et al., U.S. 5,948,903; Cook et al., U.S. 5,587,470; Cook et al., U.S. 5,457,191; Matteucci et al., U.S. 5,763,588; Froehler et al., U.S. 5,830,653; Cook et al., U.S. 5,808,027; Cook et al., 6,166,199; and Matteucci et al., U.S. 6,005,096.

3. **Certain Modified Internucleoside Linkages**

In certain embodiments, nucleosides of modified oligonucleotides may be linked together using any internucleoside linkage. The two main classes of internucleoside linking groups are defined by the presence or absence of a phosphorus atom. Representative phosphorus-containing internucleoside linkages include but are not limited to phosphodiesters, which contain a phosphodiester bond ("$P(O_2)=O$") (also referred to as unmodified or naturally occurring linkages), phosphotriesters, methylphosphonates, phosphoramidates, and phosphorothioates ("$P(O_2)=S$"), and phosphorodithioates ("HS-P=S"). Representative non-phosphorus containing internucleoside linking groups include but are not limited to methylenemethylimino ($-CH_2-N(CH_3)-O-CH_2-$), thiodiester, thionocarbamate (-O-C(=O)(NH)-S-); siloxane ($-O-SiH_2-O-$); and N,N'-dimethylhydrazine ($-CH_2-N(CH_3)-N(CH_3)-$). Modified internucleoside linkages, compared to naturally occurring 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.

Representative internucleoside linkages having a chiral center include but are not limited to alkylphosphonates and phosphorothioates. Modified oligonucleotides comprising internucleoside linkages having a chiral center can be prepared as populations of modified oligonucleotides comprising stereorandom internucleoside linkages, or as populations of modified oligonucleotides comprising phosphorothioate linkages in particular stereochemical configurations. In certain embodiments, populations of modified oligonucleotides comprise phosphorothioate internucleoside linkages wherein all of the phosphorothioate internucleoside linkages are stereorandom. Such modified oligonucleotides can be generated using synthetic methods that result in random selection of the stereochemical configuration of each phosphorothioate linkage. Nonetheless, as is well understood by those of skill in the art, each individual phosphorothioate of each individual oligonucleotide molecule has a defined stereoconfiguration. In certain embodiments, populations of modified oligonucleotides are enriched for modified oligonucleotides comprising one or more particular phosphorothioate internucleoside linkage in a particular, independently selected stereochemical configuration. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 65% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 70% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 80% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 90% of the molecules in the population. In certain embodiments, the particular configuration of the particular phosphorothioate linkage is present in at least 99% of the molecules in the population. Such chirally enriched populations of modified oligonucleotides can be generated using

synthetic methods known in the art, *e.g.*, methods described in Oka et al., *JACS* 125, 8307 (2003), Wan et al. *Nuc. Acid. Res.* 42, 13456 (2014), and WO 2017/015555. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one indicated phosphorothioate in the *(S*p*)* configuration. In certain embodiments, a population of modified oligonucleotides is enriched for modified oligonucleotides having at least one phosphorothioate in the *(R*p*)* configuration. In certain embodiments, modified oligonucleotides comprising *(R*p*)* and/or *(S*p*)* phosphorothioates comprise one or more of the following formulas, respectively, wherein "B" indicates a nucleobase:



(R_p) (S_p)

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

Neutral internucleoside linkages include, without limitation, phosphotriesters, methylphosphonates, MMI (3'-CH_2-N(CH_3)-O-5'), amide-3 (3'-CH_2-C(=O)-N(H)-5'), amide-4 (3'-CH_2-N(H)-C(=O)-5'), formacetal (3'-O-CH_2-O-5'), methoxypropyl (MOP), and thioformacetal (3'-S-CH_2-O-5'). Further neutral internucleoside linkages include nonionic linkages comprising siloxane (dialkylsiloxane), carboxylate ester, carboxamide, sulfide, sulfonate ester and amides (See for example: *Carbohydrate Modifications in Antisense Research*; Y.S. Sanghvi and P.D. Cook, Eds., ACS Symposium Series 580; Chapters 3 and 4, 40-65). Further neutral internucleoside linkages include nonionic linkages comprising mixed N, O, S and CH_2 component parts. In certain embodiments, a neutral internucleoside linkage is any of those described in WO 2021/030778, incorporated by reference herein.

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 portion 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 have 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'-deoxyribosyl sugar moiety. In certain embodiments, each nucleoside of the gap of a gapmer comprises a 2'-β-D-deoxyribosyl 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, the gapmer is a deoxy gapmer. In certain embodiments, the nucleosides on the gap side of each wing/gap junction comprise 2'-deoxyribosyl 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'-deoxyribosyl sugar moiety. In certain embodiments, each nucleoside of each wing of a gapmer comprises a modified sugar moiety. In certain embodiments, one nucleoside of the gap comprises a modified sugar moiety and each remaining nucleoside of the gap comprises a 2'-deoxyribosyl 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 5-10-5 gapmer consists of 5 linked nucleosides in each wing and 10 linked nucleosides in the gap. Where such nomenclature is followed by a specific modification, that modification is the modification in each sugar moiety of each wing and the gap nucleosides comprises a 2'-β-D-deoxyribosyl sugar moiety. Thus, a 5-10-5 MOE gapmer consists of 5 linked 2'-MOE nucleosides in the 5'-wing, 10 linked a 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 a 2'-β-D-deoxynucleosides in the gap, and 5 linked nucleosides comprising a modified sugar moiety in the 3'-wing. A 5-8-5 or 5-8-4 mixed wing 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 6-10-4 MOE gapmers. In certain embodiments, modified oligonucleotides are 5-8-4 MOE gapmers. In certain embodiments, modified oligonucleotides are X-Y-Z MOE gapmers, wherein X and Z are independently selected from 1, 2, 3, 4, 5, 6, or 7 linked 2'-MOE nucleosides and Y is selected from 7, 8, 9, 10, or 11. linked deoxynucleosides.

In certain embodiments, modified oligonucleotides have a sugar motif selected from the following (5' to 3'): eeeeddddddddkkee or eeeedydddddkkee, wherein 'd' represents a 2'-deoxyribosyl sugar moiety, 'e' represents a 2'-MOE sugar moiety, 'k' represents a cEt sugar moiety, and 'y' represents a 2'-OMe sugar moiety.

2. Certain Nucleobase Motifs

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

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

In certain embodiments, oligonucleotides having a gapmer motif comprise a nucleoside comprising a modified nucleobase. In certain such embodiments, one nucleoside comprising a modified nucleobase is in the central gap of an oligonucleotide having a gapmer motif. In certain such embodiments, the sugar moiety of said nucleoside is a 2'-deoxyribosyl 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 portion thereof in a defined pattern or motif. In certain embodiments, each internucleoside linking group is a phosphodiester internucleoside linkage ($P(O_2)=O$). In certain embodiments, each internucleoside linking group of a modified oligonucleotide is a phosphorothioate internucleoside linkage ($P(O_2)=S$). In certain embodiments, each internucleoside linkage of a modified oligonucleotide is independently selected from a phosphorothioate internucleoside linkage and phosphodiester internucleoside linkage. In certain embodiments, each phosphorothioate internucleoside linkage is independently selected from a stereorandom phosphorothioate, a *(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 such embodiments, some or all of the internucleoside linkages in the wings are unmodified phosphodiester internucleoside linkages. In certain embodiments, the terminal internucleoside linkages are modified. In certain embodiments, the sugar motif of a modified oligonucleotide is a gapmer, and the internucleoside linkage motif comprises at least one phosphodiester internucleoside linkage in at least one wing, wherein the at least one phosphodiester linkage is not a terminal internucleoside linkage, and the remaining internucleoside linkages are phosphorothioate internucleoside linkages. In certain such embodiments, all of the phosphorothioate linkages are stereorandom. In certain embodiments, all of the phosphorothioate linkages in the wings are *(S*p*)* phosphorothioates, and the gap comprises at least one *S*p, *S*p, *R*p motif. In certain embodiments, all of the internucleoside linkages are either phosphodiester internucleoside linkages or phosphorothioate internucleoside linkages, and the chiral motif is (5' to 3'): *S*p-o-o-o-*S*p-*S*p-*S*p-*R*p-*S*p-*S*p-*R*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p or *S*p-o-o-o-*S*p-*S*p-*S*p-*R*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p-*S*p, wherein each '*S*p' represents a (*S*p) phosphorothioate internucleoside linkage, each '*R*p' is a *R*p internucleoside linkage, and each 'o' represents a phosphodiester internucleoside linkage. 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 sooossssssssssssooss, 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 of (5' to 3'): sooooossssssssssoss, 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 of (5' to 3'): sssossssssssssssosss, 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 of (5' to 3'): sssossssssssssoss, wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester 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 nucleic acid 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 nucleic acid, 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 29, 19 to 28, 19 to 29, 19 to 30, 20 to 21, 20 to 22, 20 to 23, 20 to 24, 20 to 25, 20 to 26, 20 to 27, 20 to 28, 20 to 29, 20 to 30, 21 to 22, 21 to 23, 21 to 24, 21 to 25, 21 to 26, 21 to 27, 21 to 28, 21 to 29, 21 to 30, 22 to 23, 22 to 24, 22 to 25, 22 to 26, 22 to 27, 22 to 28, 22 to 29, 22 to 30, 23 to 24, 23 to 25, 23 to 26, 23 to 27, 23 to 28, 23 to 29, 23 to 30, 24 to 25, 24 to 26, 24 to 27, 24 to 28, 24 to 29, 24 to 30, 25 to 26, 25 to 27, 25 to 28, 25 to 29, 25 to 30, 26 to 27, 26 to 28, 26 to 29, 26 to 30, 27 to 28, 27 to 29, 27 to 30, 28 to 29, 28 to 30, or 29 to 30 linked nucleosides.

D. Certain Modified Oligonucleotides

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

E. Certain Populations of Modified Oligonucleotides

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

moieties, and all of the phosphorothioate internucleoside linkages are stereorandom. In certain embodiments, the modified oligonucleotides of a chirally enriched population are enriched for both β-D ribosyl sugar moieties and at least one, particular phosphorothioate internucleoside linkage in a particular stereochemical configuration.

F. Nucleobase Sequence

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

II. Certain Oligomeric Compounds

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

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

A. Certain Conjugate Groups

In certain embodiments, oligonucleotides are covalently attached to one or more conjugate groups. In certain embodiments, conjugate groups modify one or more properties of the attached oligonucleotide, including but not limited to pharmacodynamics, pharmacokinetics, stability, binding, absorption, tissue distribution, cellular distribution, cellular uptake, charge and clearance. In certain embodiments, conjugate groups impart a new property on the attached oligonucleotide, *e.g.*, fluorophores or reporter groups that enable detection of the oligonucleotide. Certain conjugate groups and conjugate moieties have been described previously, for example: cholesterol moiety (Letsinger et al., Proc. Natl. Acad. Sci. USA, 1989, 86, 6553-6556), cholic acid (Manoharan et al., *Bioorg. Med. Chem. Lett.*, 1994, *4*, 1053-1060), a thioether, *e.g.,* hexyl-S-tritylthiol (Manoharan et al., *Ann. N.Y. Acad. Sci.*, 1992, *660*, 306-309; Manoharan et al., *Bioorg. Med. Chem. Lett.,* 1993, *3*, 2765-2770), a thiocholesterol (Oberhauser et al., *Nucl. Acids Res.*, 1992, *20*, 533-538), an aliphatic chain, *e.g.,* do-decan-diol or undecyl residues (Saison-Behmoaras et al., *EMBO J.,* 1991, *10*, 1111-1118; Kabanov et al., *FEBS Lett.*, 1990, *259*, 327-330; Svinarchuk et al., *Biochimie*, 1993, *75*, 49-54), a phospholipid,

e.g., di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan et al., *Tetrahedron Lett.*, 1995, *36*, 3651-3654; Shea et al., *Nucl. Acids Res.*, 1990, *18*, 3777-3783), a polyamine or a polyethylene glycol chain (Manoharan et al., *Nucleosides & Nucleotides*, 1995, *14*, 969-973), or adamantane acetic acid a palmityl moiety (Mishra et al., *Biochim. Biophys. Acta*, 1995, *1264,* 229-237), an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke et al., *J. Pharmacol. Exp. Ther.,* 1996, *277*, 923-937), a tocopherol group (Nishina et al., *Molecular Therapy Nucleic Acids*, 2015**,** *4*, e220; and Nishina et al., *Molecular Therapy,* 2008, *16*, 734-740), or a GalNAc cluster (*e.g.*, WO2014/179620).

1. **Conjugate Moieties**

Conjugate moieties include, without limitation, intercalators, reporter molecules, polyamines, polyamides, peptides, carbohydrates, vitamin moieties, polyethylene glycols, thioethers, polyethers, cholesterols, thiocholesterols, cholic acid moieties, folate, lipids, lipophilic groups, phospholipids, biotin, phenazine, phenanthridine, anthraquinone, adamantane, acridine, fluoresceins, rhodamines, coumarins, fluorophores, and dyes.

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

2. **Conjugate Linkers**

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

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

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

Examples of conjugate linkers include but are not limited to pyrrolidine, 8-amino-3,6-dioxaoctanoic acid (ADO), succinimidyl 4-(N-maleimidomethyl) cyclohexane-1-carboxylate (SMCC) and 6-aminohexanoic acid (AHEX or AHA). Other conjugate linkers include but are not limited to substituted or unsubstituted C_1-C_{10} alkyl, substituted or

unsubstituted C_2-C_{10} alkenyl or substituted or unsubstituted C_2-C_{10} alkynyl, wherein a nonlimiting list of preferred substituent groups includes hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl and alkynyl.

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

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

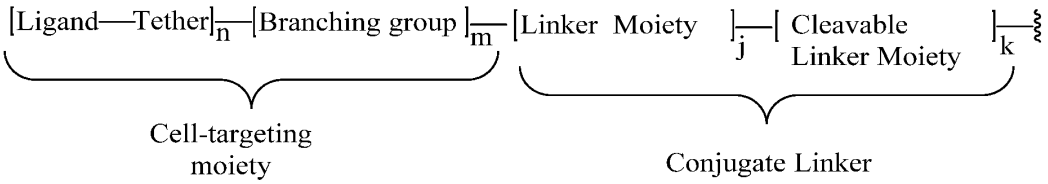
In certain embodiments, it is desirable for a conjugate group to be cleaved from the oligonucleotide. For example, in certain circumstances oligomeric compounds comprising a particular conjugate moiety are better taken up by a particular cell type, but once the oligomeric compound has been taken up,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

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

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 nucleosides and/or inverted nucleosides. In certain embodiments, terminal groups comprise one or more 2'-linked nucleosides. In certain such embodiments, the 2'-linked nucleoside is an abasic nucleoside.

III. Oligomeric Duplexes

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

IV. Antisense Activity

In certain embodiments, oligomeric compounds and oligomeric duplexes are capable of hybridizing to a target nucleic acid, resulting in at least one antisense activity; such oligomeric compounds and oligomeric duplexes are antisense compounds. In certain embodiments, antisense compounds have antisense activity when they reduce the amount or activity of a target nucleic acid by 25% or more in the standard cell assay. In certain embodiments, antisense compounds selectively affect one or more target nucleic acid. Such antisense compounds comprise a nucleobase sequence that hybridizes to one or more target nucleic acid, resulting in one or more desired antisense activity and does not hybridize to one or more non-target nucleic acid or does not hybridize to one or more non-target nucleic acid in such a way that results in significant undesired antisense activity.

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

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

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

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

V. Certain Target Nucleic Acids

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide comprising a portion 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 nucleic acid is a mature mRNA. In certain embodiments, the target nucleic acid is a pre-mRNA. In certain such embodiments, the target region is entirely within an intron. In certain embodiments, the target region spans an intron/exon junction. In certain embodiments, the target region is at least 50% within an intron.

A. Complementarity/Mismatches to the Target Nucleic Acid

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

In certain embodiments, oligonucleotides 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 portion that is 100% or fully complementary to a target nucleic acid. In certain embodiments, the portion of full complementarity is 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, or 24 nucleobases in length.

In certain embodiments, oligonucleotides comprise one or more mismatched nucleobases relative to the target nucleic acid. In certain embodiments, antisense activity against the target is reduced by such mismatch, but activity against a non-target is reduced by a greater amount. Thus, in certain embodiments selectivity of the oligonucleotide is improved. In certain embodiments, the mismatch is specifically positioned within an oligonucleotide having a gapmer motif. In certain embodiments, the mismatch is at position 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, or 11 from the 5'-end of the gap region. In certain embodiments, the mismatch is at position 1, 2, 3, 4, 5, or 6 from the 5'-end of the 5' wing region or the 3' wing region.

B. ATXN1

In certain embodiments, oligomeric compounds comprise or consist of an oligonucleotide that is complementary to a target nucleic acid, wherein the target nucleic acid is an ATXN1 nucleic acid. In certain embodiments, ATXN1 nucleic acid has the sequence set forth in SEQ ID NO: 1 (GENBANK Accession No. NM_000332.3), SEQ ID NO: 2 (the complement of GENBANK Accession No. NC_000006.12 truncated from nucleotides 16296001to 16764000), SEQ ID NO: 3 (GENBANK Accession No. NM_001128164.1), SEQ ID NO: 4 (GENBANK Accession No. BC011026.1), SEQ ID NO: 5 (GENBANK Accession No. BC029401.1), or SEQ ID NO: 6 (GENBANK Accession No. BC047894.1).

In certain embodiments, contacting a cell with an oligomeric compound complementary to any of SEQ ID NO: 1-6 reduces the amount of ATXN1 RNA in a cell. In certain embodiments, contacting a cell with an oligomeric compound complementary to any of SEQ ID NO: 1-6 reduces the amount of ATXN1 in a 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 any of SEQ ID NO: 1-6 ameliorates one or more symptom or hallmark of a neurodegenerative disease. In certain embodiments, the neurodegenerative disease is SCA1. In certain embodiments, the symptom or hallmark is selected from gait and limb ataxia, cognitive impairments, difficulty with speaking and swallowing, atrophy of the cerebellum and brainstem in magnetic resonance imaging (MRI), neurochemical abnormalities in the cerebellum and brainstem detected via magnetic resonance spectroscopy (MRS), and death within 10-15 years of symptom onset.

In certain embodiments, an oligomeric compound complementary to any of SEQ ID NO: 1-6 is capable of reducing the detectable amount of ATXN1 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 cell assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 is capable of decreasing the amount of ATXN1 *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 cell assay. In certain embodiments, an oligomeric compound complementary to SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 is capable of reducing the detectable amount of ATXN1 RNA in the CSF 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, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, or SEQ ID NO: 6 is capable of decreasing the detectable amount of ATXN1 in the CSF 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 portion that is complementary to a target nucleic acid, wherein the target nucleic acid is expressed in a pharmacologically relevant tissue. In certain embodiments, the pharmacologically relevant tissues are the cells and tissues that comprise the central nervous system. Such tissues include the cortex, cerebellum, and brainstem.

VI. Certain Pharmaceutical Compositions

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

pharmaceutical composition comprises or consists of one or more oligomeric compound and artificial cerebrospinal fluid. In certain embodiments, the artificial cerebrospinal fluid is pharmaceutical grade.

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

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

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

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

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

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

In certain embodiments, pharmaceutical compositions comprise one or more tissue-specific delivery molecules designed to deliver the one or more pharmaceutical agents comprising an oligomeric compound provided herein 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.

VII. Certain Compositions

1. Compound No. 994509

In certain embodiments, Compound No. 994509 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GCACGGTATTAGTGTCTTCA (SEQ ID NO: 126), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 994509 is represented by the following chemical notation (5' to 3'): Ges ^{m}Ceo Aeo ^{m}Ceo Ges Gds Tds Ads Tds Tds Ads Gds Tds Gds Tds ^{m}Ceo Teo Tes ^{m}Ces Ae (SEQ ID NO: 126), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

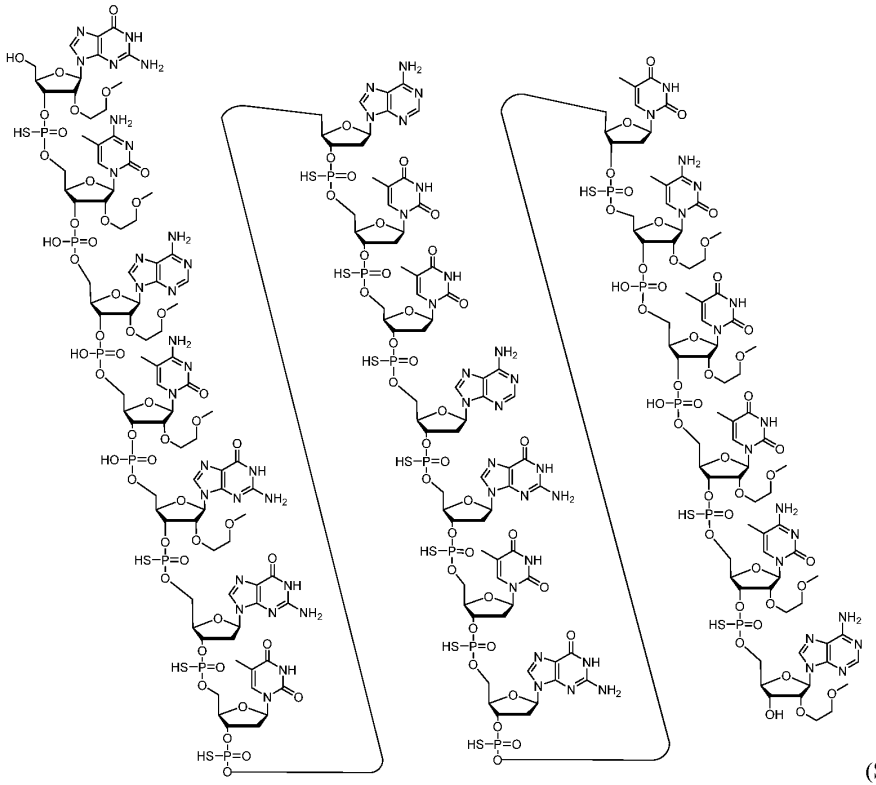
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

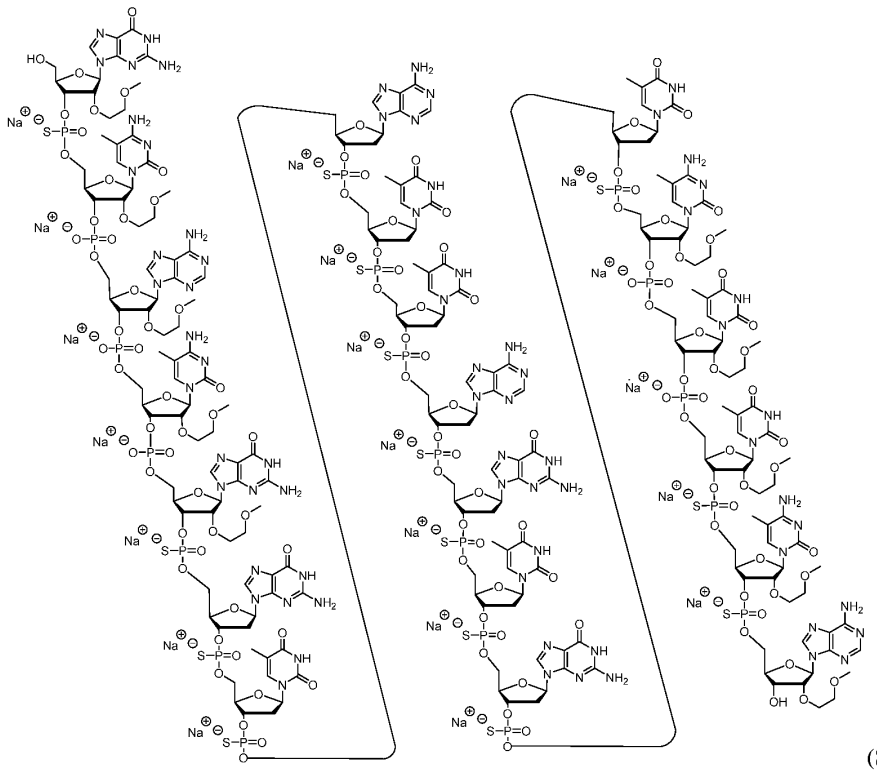
In certain embodiments, Compound No. 994509 is represented by the following chemical structure:



(SEQ ID NO: 126).

Structure 1. Compound No. 994509

In certain embodiments, the sodium salt of Compound No. 994509 is represented by the following chemical structure:



(SEQ ID NO: 126).

Structure 2. The sodium salt of Compound No. 994509

2. Compound No. 1040500

In certain embodiments, Compound No. 1040500 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GCTTCTCAAATCAGGTGTAC (SEQ ID NO: 1045), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1040500 is represented by the following chemical notation (5' to 3'): Ges ^{m}Ceo Teo Teo ^{m}Ces Tds ^{m}Cds Ads Ads Ads Tds ^{m}Cds Ads Gds Gds Teo Geo Tes Aes mCe (SEQ ID NO: 1045), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

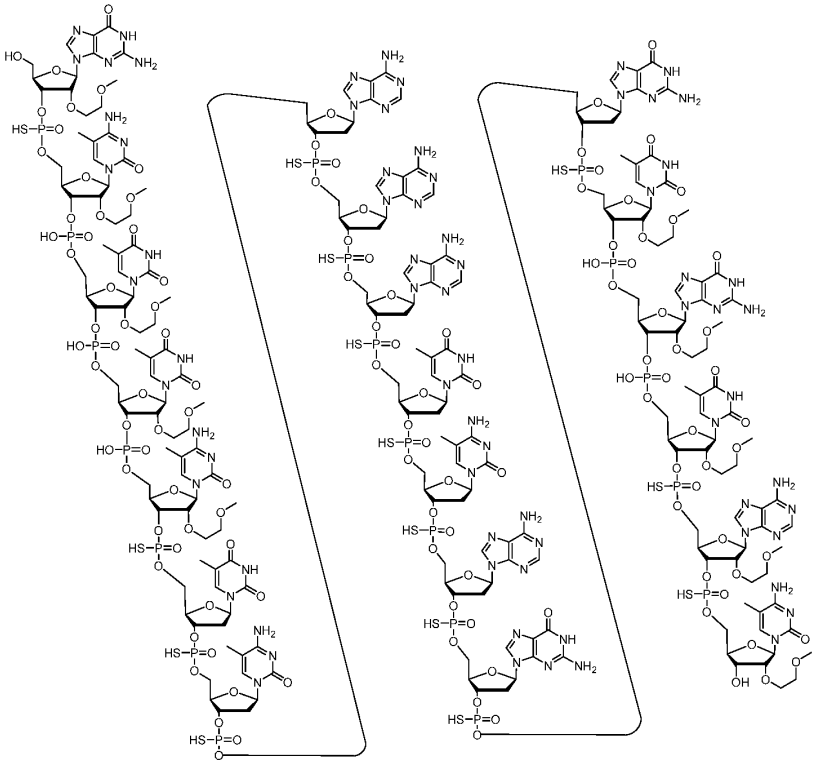
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

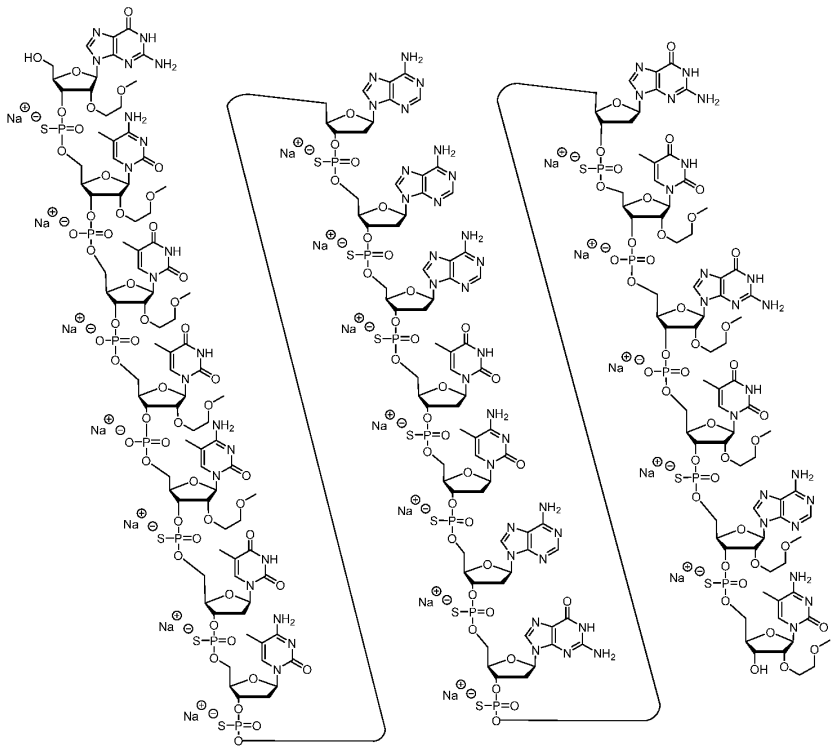
In certain embodiments, Compound No. 1040500 is represented by the following chemical structure:



(SEQ ID NO: 1045).

Structure 3. Compound No. 1040500

In certain embodiments, the sodium salt of Compound No. 1040500 is represented by the following chemical structure:



(SEQ ID NO: 1045).

Structure 4. The sodium salt of Compound No. 1040500

3. Compound No. 1041927

In certain embodiments, Compound No. 1041927 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') GCCTTTATAACTTTTCTTTC (SEQ ID NO: 2552), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1041927 is represented by the following chemical notation (5' to 3'): Ges ^{m}Ceo ^{m}Ceo Teo Tes Tds Ads Tds Ads Ads ^{m}Cds Tds Tds Tds Tds ^{m}Ceo Teo Tes Tes ^{m}Ce (SEQ ID NO: 2552), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

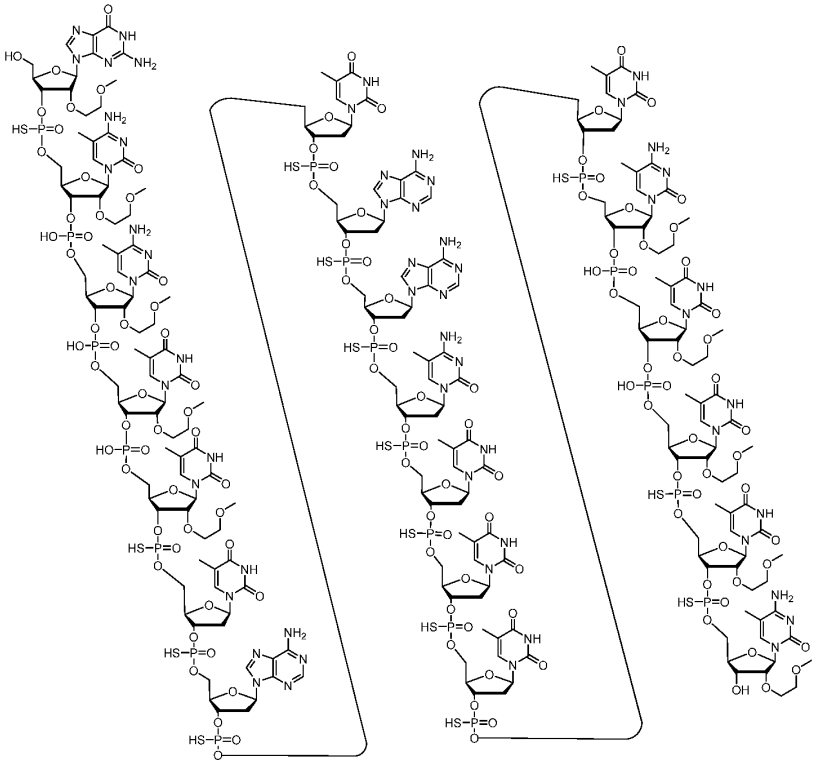
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

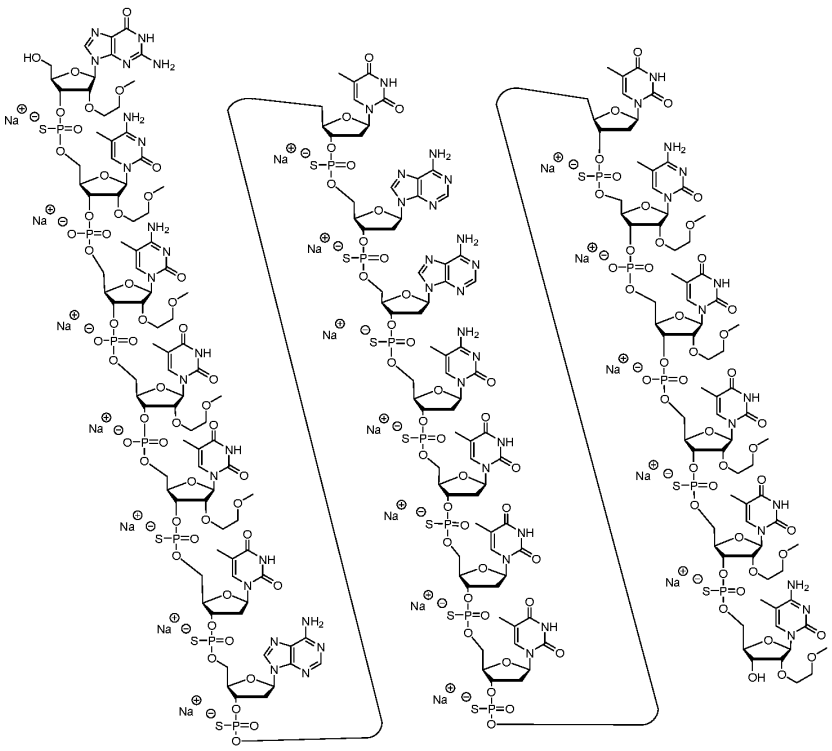
In certain embodiments, Compound No. 1041927 is represented by the following chemical structure:



(SEQ ID NO: 2552).

Structure 5. Compound No. 1041927

In certain embodiments, the sodium salt of Compound No. 1041927 is represented by the following chemical structure:



(SEQ ID NO: 2552).

Structure 6. The sodium salt of Compound No. 1041927

4. Compound No. 1055001

In certain embodiments, Compound No. 1055001 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') TTCAGTTTAGTTGCAGCCAT (SEQ ID NO: 3190), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1055001 is represented by the following chemical notation (5' to 3'): Tes Teo ^{m}Ceo Aeo Ges Tds Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Ads Geo ^{m}Ceo ^{m}Ces Aes Te (SEQ ID NO: 3190), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

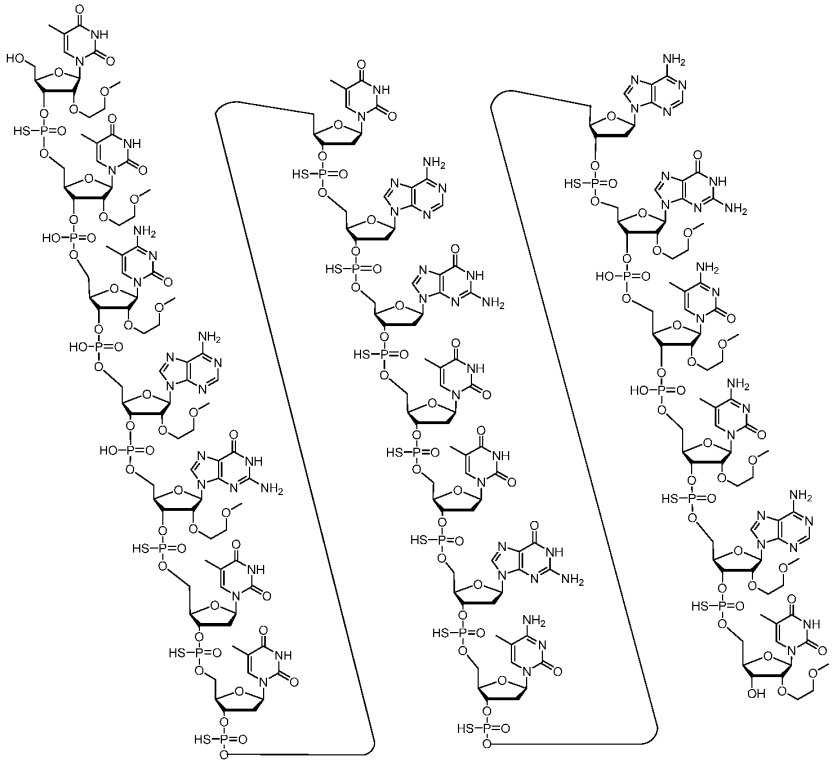
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

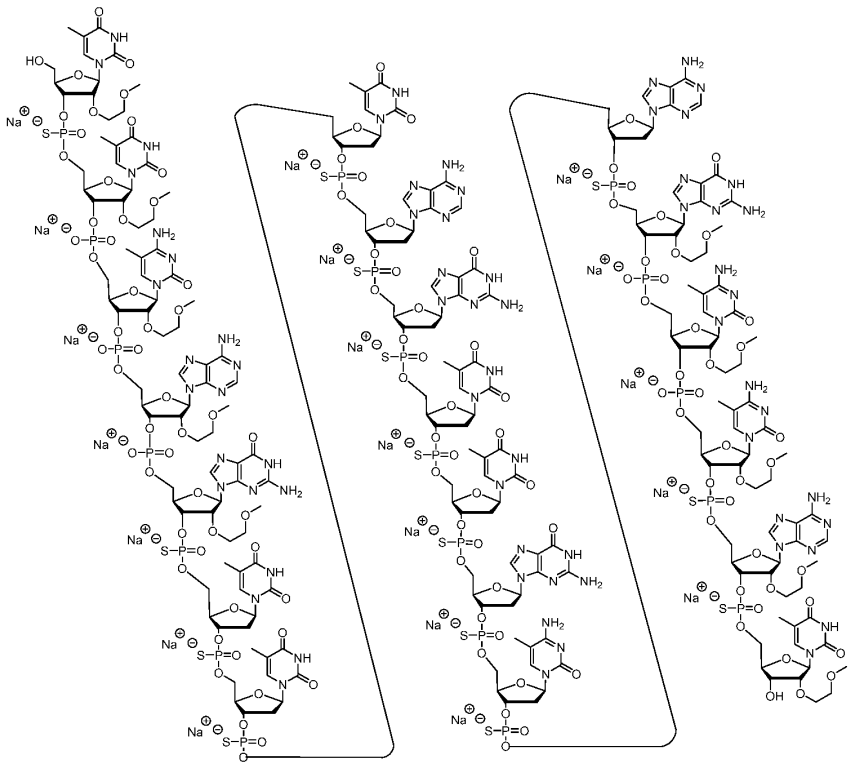
In certain embodiments, Compound No. 1055001 is represented by the following chemical structure:



(SEQ ID NO: 3190).

Structure 7. Compound No. 1055001

In certain embodiments, the sodium salt of Compound No. 1055001 is represented by the following chemical structure:



(SEQ ID NO: 3190).

Structure 8. The sodium salt of Compound No. 1055001

5. Compound No. 1371311

In certain embodiments, Compound No. 1371311 is characterized as a 5-10-5 MOE gapmer having a sequence of (from 5' to 3') CCCGTATTCCTCTTACCATC (SEQ ID NO: 3590), wherein each of nucleosides 1-5 and 16-20 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-15 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 2 to 3, 3 to 4, 4 to 5, 16 to 17, and 17 to 18 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 14 to 15, 15 to 16, 18 to 19, and 19 to 20 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1371311 is represented by the following chemical notation (5' to 3'): ^{m}Ces ^{m}Ceo ^{m}Ceo Geo Tes Ads Tds Tds ^{m}Cds ^{m}Cds Tds ^{m}Cds Tds Tds Ads ^{m}Ceo ^{m}Ceo Aes Tes ^{m}Ce (SEQ ID NO: 3590), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

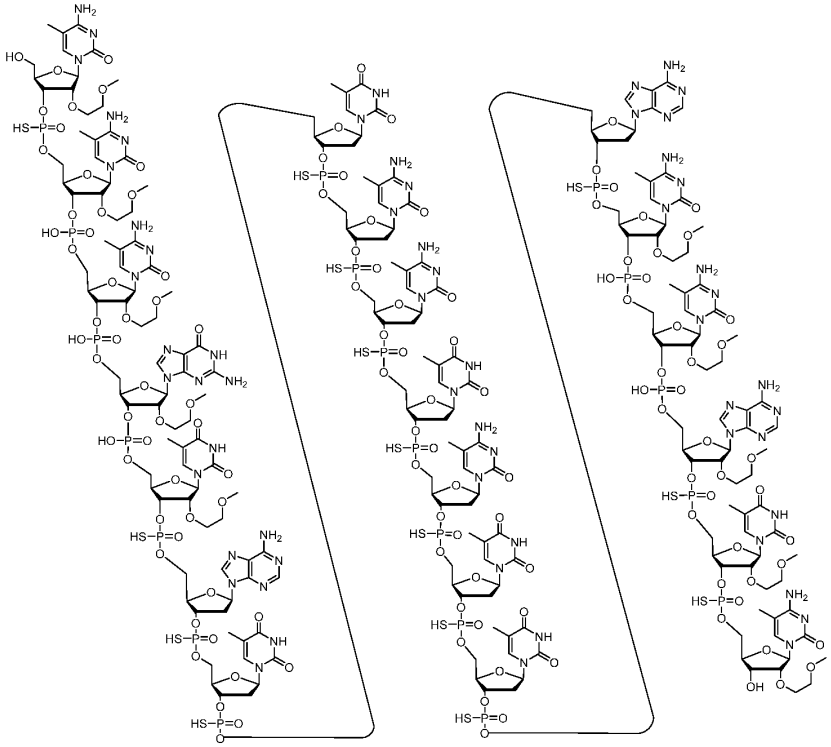
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

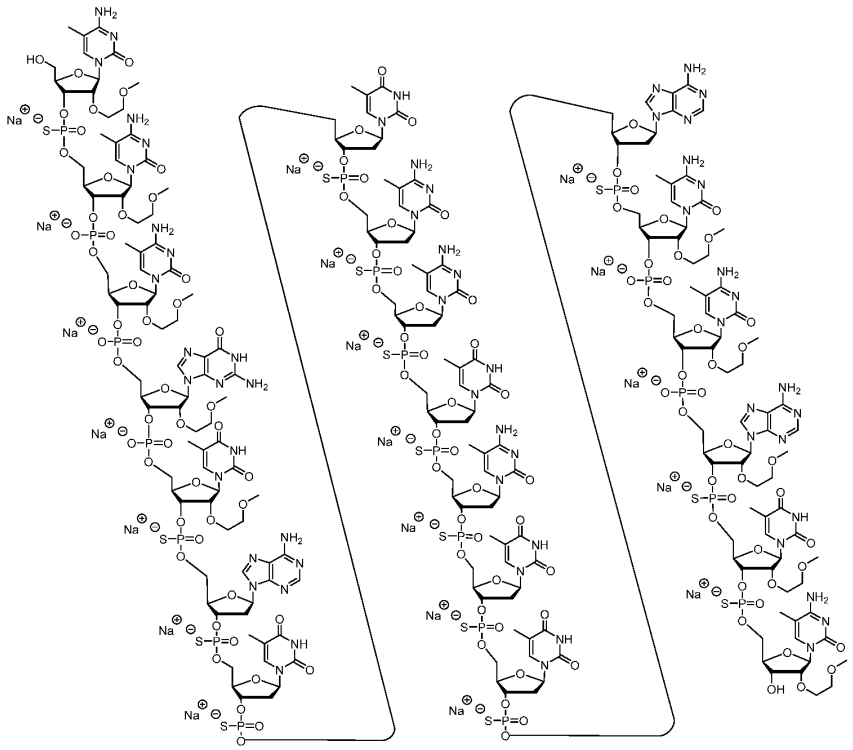
In certain embodiments, Compound No. 1371311 is represented by the following chemical structure:



(SEQ ID NO: 3590).

Structure 9. Compound No. 1371311

In certain embodiments, the sodium salt of Compound No. 1371311 is represented by the following chemical structure:



(SEQ ID NO: 3590).

Structure 10. The sodium salt of Compound No. 1371311

6. Compound No. 1385293

In certain embodiments, Compound No. 1385293 is characterized as a 5-8-4 MOE gapmer having a sequence of (from 5' to 3') TCAGTTTAGTTGCAGCC (SEQ ID NO: 3638), wherein each of nucleosides 1-5 and 14-17 (from 5' to 3') are 2'-MOE nucleosides and each of nucleosides 6-13 are 2'-β-D-deoxynucleosides, wherein the internucleoside linkages between nucleosides 4 to 5 and 14 to 15 are phosphodiester internucleoside linkages and the internucleoside linkages between nucleosides 1 to 2, 3 to 4, 5 to 6, 6 to 7, 7 to 8, 8 to 9, 9 to 10, 10 to 11, 11 to 12, 12 to 13, 13 to 14, 15 to 16, and 16 to 17 are phosphorothioate internucleoside linkages, and wherein each cytosine is a 5-methyl cytosine.

In certain embodiments, Compound No. 1385293 is represented by the following chemical notation (5' to 3'): Tes ^{m}Ces Aes Geo Tes Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Aeo Ges ^{m}Ces ^{m}Ce (SEQ ID NO: 3638), wherein,

A = an adenine nucleobase,

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

G = a guanine nucleobase,

T = a thymine nucleobase,

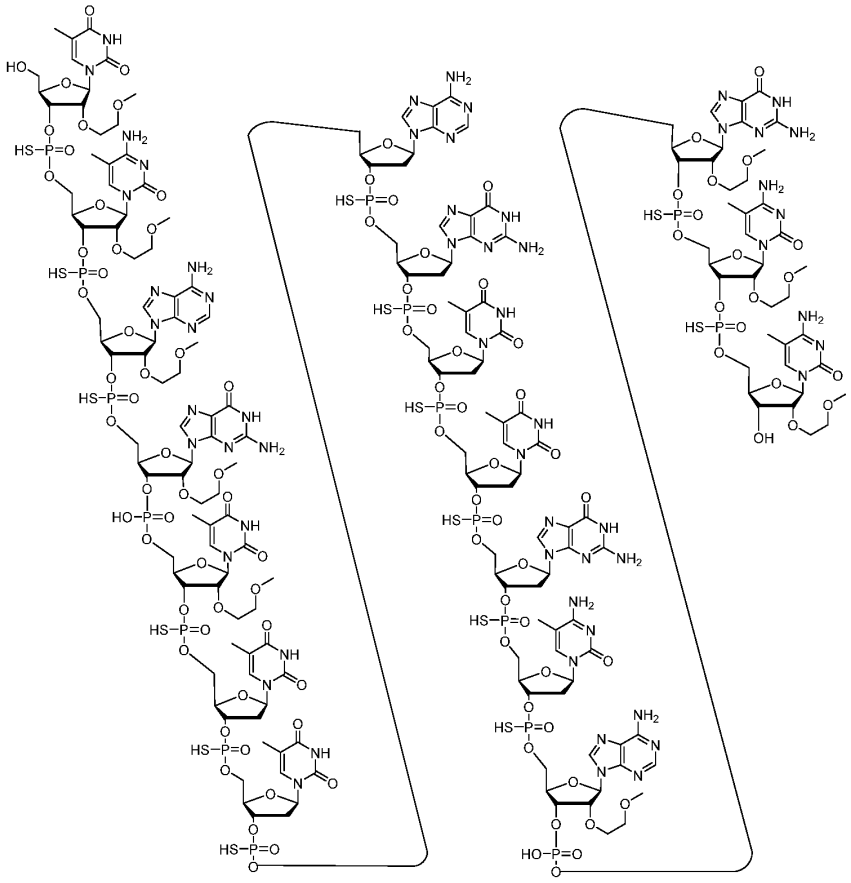
e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

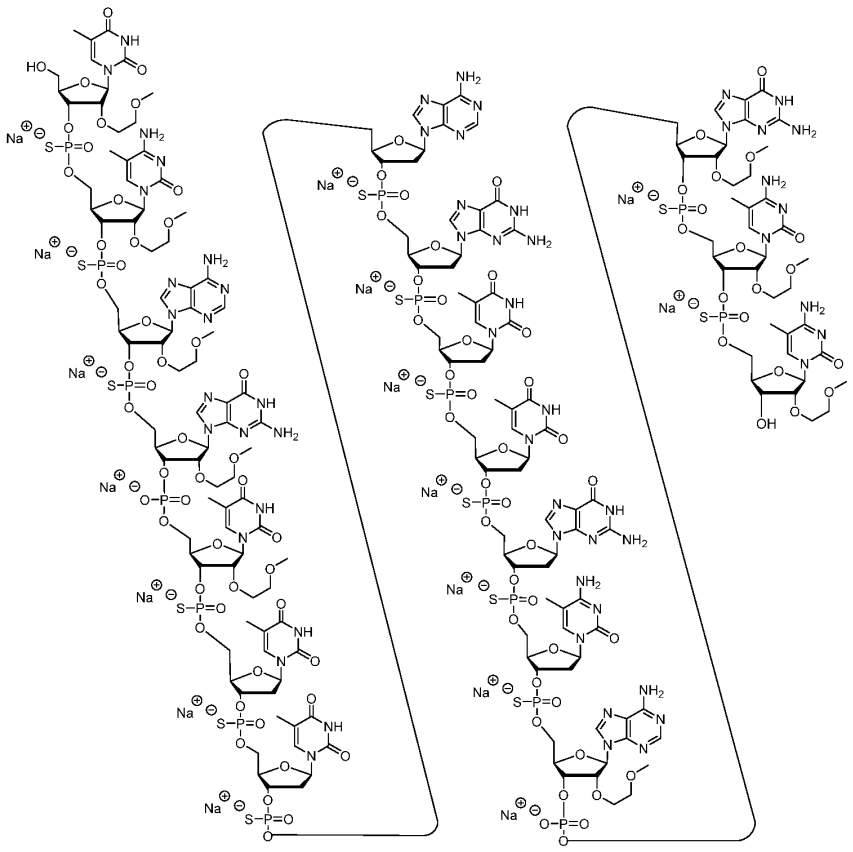
In certain embodiments, Compound No. 1385293 is represented by the following chemical structure:



(SEQ ID NO: 3638).

Structure 11. Compound No. 1385293

In certain embodiments, the sodium salt of Compound No. 1385293 is represented by the following chemical structure:



(SEQ ID NO: 3638).

Structure 12. The sodium salt of Compound No. 1385293

VIII. Certain Hotspot Regions

In certain embodiments, nucleobases in the ranges specified below comprise a hotspot region of ATXN1 nucleic acid. In certain embodiments, modified oligonucleotides that are complementary within a hotspot region of ATXN1 nucleic acid achieve an average of more than 75% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides that are complementary within a hotspot region of ATXN1 nucleic acid achieve an average of 24% or greater reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay. In certain embodiments, modified oligonucleotides that are complementary within a hotspot region of ATXN1 nucleic acid achieve an average of 45% or greater reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay.

1. Nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2

In certain embodiments, nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, modified oligonucleotides are mixed wing gapmers.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-

4 MOE gapmers. In certain embodiments, the gapmers are 5-8-4 MOE gapmers or 5-8-4 mixed MOE/cEt gapmers. In certain embodiments, the mixed wing gapmers have the sugar motif in order from 5' to 3': eeeeddddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, and 'e' represents a 2'-MOE sugar moiety. In certain embodiments, the gapmers comprise a 2'-substituted nucleoside in the gap. In certain embodiments, the 2'-substituted nucleoside comprises a 2'-OMe sugar moiety. In certain embodiments, the 2'-substituted nucleoside is at position 2 of the gap (5' to 3'). In certain embodiments, the gapmers have the sugar motif in order from 5' to 3': eeeeedyddddddddeeeee or eeeeedyddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, 'e' represents a 2'-MOE sugar moiety, and "y" represents a 2'-OMe 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 nucleotides have an internucleoside linkage motif of sooossssssssssssooss, sssossssssssssssosss, sssossssssssssoss, or sooooossssssssssoss wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID Nos: 196, 274, 352, 430, 508, 2578, 2655, 2732, 2809, 2886, 2963, 3121, 3122, 3190, 3191, 3192, 3262, 3330, 3331, 3332, 3401, 3402, 3575, 3577, 3620, 3624, 3638-3640, 3653-3655, 3662, 3665, and 3669 are complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2.

The nucleobase sequence of Compound Nos.: 994446-994450, 1040296-1040301, 1055001-1055011, 1342062, 1342063, 1342067, 1342068, 1365271, 1365272, 1365274, 1365294, 1365299, 1365300, 1371818, 1371821, 1371827, 1371829, 1371837,1371843, 1371866, 1371869, 1371871, 1371876, 1385293, 1394156-1394160, 1394162, 1394164, 1394166-1394168, 1394533, 1394544, 1394546, 1394549, and 1394553 are complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2 achieve at least 58% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2 achieve an average of 90% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 5472-5552 of SEQ ID NO: 1 or 459725-459805 of SEQ ID NO: 2 achieve an average of 52% reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay.

2. <u>Nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2</u>

In certain embodiments, nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are mixed wing gapmers.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-4 MOE gapmers. In certain embodiments, the gapmers are 5-8-4 MOE gapmers or 5-8-4 mixed MOE/cEt gapmers. In certain embodiments, the mixed wing gapmers have the sugar motif in order from 5' to 3': eeeeddddddddkkee; wherein

'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, and '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 nucleotides have an internucleoside linkage motif of sooosssssssssssooss, sssosssssssssssosss, sssosssssssssoss, or sooooosssssssssssoss wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID Nos: 42, 120, 198, 276, 509, 587, 2502, 2579, 2656, 2733, 2810, 2887, 2964, 3585, 3588-3590, 3615, 3618, 3622, 3657, 3660, 3661, 3663, 3664, and 3666-3668 are complementary within nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2.

The nucleobase sequence of Compound Nos.: 994458-994463, 1040327-1040333, 1367569, 1367580-1367581, 1367589-1367591, 1371311, 1371820, 1371823, 1371825, 1371842, 1371865, 1371868, 1371870, 1371873, 1371875, 1371877, 1394161, 1394163, 1394165, 1394524, 1394538, 1394541, 1394543, 1394545, 1394548, and 1394550-1394552 are complementary within nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary within 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2 achieve at least 26% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2 achieve an average of 78% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 5906-6005 of SEQ ID NO: 1 or 460159-460258 of SEQ ID NO: 2 achieve an average of 51% reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay.

3. <u>Nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2</u>

In certain embodiments, nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-4 MOE gapmers.

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 nucleotides have an internucleoside linkage motif of sooosssssssssssooss, sssosssssssssssosss, or sooooosssssssssssoss wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID Nos: 48, 126, 2044, and 2121 are complementary within nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2.

The nucleobase sequence of Compound Nos.: 994508, 994509, 1040499, 1040450, 1394513, and 1394529 are complementary within nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary within 7868-7911 of SEQ ID NO: 1 or 462121-462145 of SEQ ID NO: 2 achieve at least 61% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462145 of SEQ ID NO: 2 an average of 79% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 7868-7911 of SEQ ID NO: 1 or 462121-462164 of SEQ ID NO: 2 achieve an average of 53% reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay.

4. Nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2

In certain embodiments, nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-4 MOE gapmers.

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 nucleotides have an internucleoside linkage motif of sooosssssssssssooss, sssossssssssssosss, or soooooossssssssssoss wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID Nos: 128, 206, 284, 1045, 1122, 1199, and 1276 are complementary within nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2.

The nucleobase sequence of Compound Nos.: 994525-994527, 1040500-1040503, 1394514, and 1394525 are complementary within nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary within 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2 achieve at least 54% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2 achieve an average of 79% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 8481-8514 of SEQ ID NO: 1 or 462734-462767 of SEQ ID NO: 2 achieve an average of 48% reduction of ATXN1 RNA *in vivo* in the standard *in vivo* assay.

5. Nucleobases 446679-446706 of SEQ ID NO: 2

In certain embodiments, nucleobases 446679-446706 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary to nucleobases 446679-446706 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-4 MOE gapmers.

In certain embodiments, 446679-446706 of SEQ ID NO: 2 comprise a hotspot region. In certain embodiments, modified oligonucleotides are complementary within 446679-446706 of SEQ ID NO: 2. In certain embodiments, modified oligonucleotides are 20 nucleobases in length. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are gapmers. In certain embodiments, the gapmers are MOE gapmers. In certain embodiments, the internucleoside linkages of the modified oligonucleotides are phosphorothioate internucleoside linkages and phosphodiester internucleoside linkages. In certain embodiments, the phosphodiester ("o") and phosphorothioate ("s") internucleoside linkages are arranged in order from 5' to 3': In certain embodiments, modified nucleotides have an internucleoside linkage motif of sooosssssssssssooss, ssssossssssssssosss, or soooooossssssssssoss wherein each "s" represents a phosphorothioate internucleoside linkage and each "o" represents a phosphodiester internucleoside linkage.

The nucleobase sequences of SEQ ID Nos: 2475, 2552, 2629, 2706, 2783, 3627-3630, and 3644 are complementary within nucleobases 446679-446706 of SEQ ID NO: 2.

The nucleobase sequence of Compound Nos.: 1041926-1041930, 1364282, 1365258-1365261, 1365282-1365284, 1365287, and 1394522 are complementary within nucleobases 446679-446706 of SEQ ID NO: 2.

In certain embodiments, modified oligonucleotides complementary within nucleobases 446679-446706 of SEQ ID NO: 2 achieve at least 67% reduction of ATXN1 RNA *in vitro* in the standard cell assay. In certain embodiments, modified oligonucleotides complementary within nucleobases 446679-446706 of SEQ ID NO: 2.achieve an average of 81% reduction of ATXN1 RNA *in vitro* in the standard cell assay.

6. Additional Hotspot Regions

In certain embodiments, the 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, modified oligonucleotides are complementary within any of the hotspot regions 1-53, as defined in the table below. In certain embodiments, modified oligonucleotides are 17 nucleobases in length. In certain embodiments, modified oligonucleotides are 20 nucleobases in length.

In certain embodiments, the gapmers are 5-10-5 MOE gapmers. In certain embodiments, the gapmers are 6-10-4 MOE gapmers. In certain embodiments, the gapmers are 5-8-4 MOE gapmers or 5-8-4 mixed MOE/cEt gapmers. In certain embodiments, the mixed wing gapmers have the sugar motif in order from 5' to 3': eeeeddddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, and 'e' represents a 2'-MOE sugar moiety. In certain embodiments, gapmers comprise a 2'-substituted nucleoside in the gap. In certain embodiments, the 2'-substituted nucleoside comprises a 2'-OMe sugar moiety. In certain embodiments, the 2'-substituted nucleoside is at position 2 of the gap (5' to 3'). In certain embodiments, the gapmers have the sugar motif in order from 5' to 3': eeeeedyddddddddeeeee or eeeeedyddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, 'e' represents a 2'-MOE sugar moiety, and "y" represents a 2'-OMe 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 nucleotides have an internucleoside linkage motif of sooosssssssssssooss, sssossssssssssosss, sssossssssssoss,

or sooooossssssssssoss 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: 2 within the specified hotspot region. The nucleobase sequence of the oligonucleotides listed in the "SEQ ID NO: in range" column in the table below are complementary to the target sequence, SEQ ID NO: 2, within the specified hotspot region.

In certain embodiments, modified oligonucleotides complementary to nucleobases within the hotspot region achieve at least "Min.% Red. *in vitro*" (minimum % reduction, relative to untreated control cells) of ATXN1 RNA *in vitro* in the standard cell 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. *in vitro*" (average % reduction, relative to untreated control cells) of ATXN1 RNA *in vitro* in the standard cell assay, as indicated in the table below. In certain embodiments, modified oligonucleotides complementary to nucleobases within the hotspot region achieve a maximum of "Max. % Red. *in vitro*" (maximum % reduction, relative to untreated control cells) of ATXN1 RNA *in vitro* in the standard cell 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. *in vivo*" (average % reduction, relative to PBS-treated animals) of ATXN1 RNA *in vivo* in the standard *in vivo* assay in cortical tissue, as indicated in the table below. Note that due to the transgenic mouse model used, only compounds targeting nucleosides 435531-464889 of SEQ ID NO: 2 were tested *in vivo;* "n.d." indicates that no *in vivo* data are available for compounds within that range. In other cases, average reduction *in vivo* includes a subset of the compounds in any given hotspot, as not all compounds were tested *in vivo.*

Table 1

ATXN1 Hotspots

Hot spot ID	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Min. % Red. *in vitro*	Max. % Red. *in vitro*	Avg. % Red. *in vitro*	Avg. % Red. *in vivo (ctx)*	Compound No. in range	SEQ ID NO in range
1	5477	5552	459730	459805	58	96	90	54	994446-994450, 1040296-1040301, 1055001-1055011, 1342062, 1342067, 1365271, 1365272, 1365274, 1365294, 1365299-1365300, 1371818, 1371827, 1371829, 1371837, 1371843,1371871, 1371876, 1385293, 1394156-1394160, 1394162, 1394164, 1394166-1394168, 1394533, 1394544, 1394546, 1394549, 1394553	196, 274, 352, 430, 508, 2578, 2655, 2732, 2809, 2886, 2963, 3121, 3122, 3190-3192, 3262, 3330-3332, 3401, 3402, 3575, 3577, 3620, 3624, 3638-3640, 3653-3655, 3662, 3665, 3669
2	5906	6005	460159	460258	26	97	78	51	994458-994463, 1040327-1040333,	42, 120, 198, 276, 509, 587,

									1367569, 1367580-1367581, 1367589-1367591, 1371311, 1371820, 1371823, 1371825, 1371842, 1371865, 1371868, 1371870, 1371873, 1371875, 1371877, 1394161, 1394163, 1394165, 1394524, 1394538, 1394541, 1394543, 1394545, 1394548, 1394550-1394552	2502, 2579, 2656, 2733, 2810, 2887, 2964, 3585, 3588-3590, 3615, 3618, 3622, 3657, 3660, 3661, 3663, 3664, 3666-3668
3	7868	7911	462121	462145	61	94	79	53	994508, 994509, 1040499, 1040450, 1394513, 1394529	48, 126, 2044, 2121
4	8481	8514	462734	462767	54	89	79	48	994525-994527, 1040500-1040503, 1394514, 1394525	128, 206, 284, 1045, 1122, 1199, 1276
5	N/A	N/A	446679	446706	67	89	81	24	1041926-1041930, 1364282, 1365258-1365261, 1365282-1365284, 1365287, 1394522	2475, 2552, 2629, 2706, 2783, 3627-3630, 3644
6	99	140	2609	2650	43	90	76	n.d.	994310-994313, 1054946-1054957	179, 257, 335, 413, 3111-3113, 3183, 3253-3254, 3321-3322, 3394-3395, 3464-3465
7	195	227	9911	9943	64	92	78	n.d.	994597-994601, 1055055-1055061	137, 215, 293, 371, 449, 3131-3132, 3201, 3341-3342, 3410, 3478
8	243	275	10654	10686	75	93	85	n.d.	994314, 1054962-1054971	491, 3114, 3184-3185, 3255-3256, 3323-3324, 3396, 3466-3467
9	413	454	106155	106196	68	95	86	n.d.	994318-994324	25, 180, 258, 336, 414, 492, 570
10	500	589	178110	178199	60	98	88	n.d.	994325-994328, 1054972-1054984	103, 181, 259, 337, 3115-3117, 3186-3187, 3257-3258, 3325-3326, 3397-3398, 3468-3469
11	587	619	N/A	N/A	80	99	94	n.d.	994329, 1054990-1054999	415, 3119, 3188-3189, 3260-3261,

										3328-3329, 3400, 3471-3472
12	3984	4031	458237	458284	77	95	83	24	994408-994409, 1040170-1040173	347, 425, 2728, 2805, 2882, 2959, 3036
13	4434	4457	458687	458710	88*	88*	88*	49	994419, 1342032, 1364280, 1365267, 1365268, 1365270, 1365290-1365292, 1365298, 1371322, 1371325, 1371809, 1371824, 1371851, 1371854, 1371872, 1385295,1394153-1394155, 1394534, 1394537, 1394539, 1394540, 1394547	582, 3563, 3593, 3605, 3621, 3635-3637, 3648-3649, 3652, 3656, 3658-3659
14	4497	4553	458750	458806	48	91	78	25	1040205-1040211	651, 728, 805, 882, 959, 2960, 3037
15	4586	4640	458839	458893	63	99	87	50	994420-994422, 1040212-1040215	37, 115, 193, 1036, 1113, 1190, 1267
16	4725	4786	458978	459039	24	98	77	33	994429-994430, 1040222-1040239, 1342061, 1342064, 1342069, 1342071, 1342074-1342076, 1364283, 1365262-1356265, 1365285-1365286, 1365288-1365289, 1371808, 1371810, 1371813, 1371815-1371816, 1371819, 1371822, 1371844-1371845, 1371848, 1371853, 1385294, 1394507, 1394511, 1394518, 1394523, 1394527	116, 194, 652, 1806, 1883, 1960, 2037, 2114, 2191, 2268, 2345, 2422, 2499, 2576, 2653, 2730, 2807, 2884, 2961, 3038, 3558, 3560-3562, 3574, 3576, 3578, 3592, 3594, 3597, 3604, 3631-3635, 3645, 3646-3647
17	6015	6099	460268	460352	58	94	78	34	994464-994469, 1040334-1040344, 1055012-1055023, 1342039, 1342041, 1342044, 1342046, 1342048	43, 121, 354, 432, 510, 588, 655, 732, 809, 886, 963, 1040, 1117, 1194, 1271, 1348, 3041, 3123-3125, 3193-3194, 3263-3264, 3333-3334, 3403, 3473-3474, 3541, 3543, 3545, 3565, 3569

18	6919	6960	461172	461213	90	96	93	50	994484, 1040382-1040384	45, 1811, 1888, 1965
19	7076	7114	461329	461367	76	98	89	58	994490-994496, 1040393-1040395, 1394166-1394167, 1394516, 1394530	46, 124, 202, 280, 358, 513, 591,2658, 2735, 2812
20	7696	7741	461949	461994	74	94	87	29	994506, 1040435-1040438	515, 966, 1043, 1120, 1197
21	8194	8257	462447	462510	58	97	82	37	994516-994521, 1040472-1040482, 1394512, 1394517, 1394528, 1394531	49, 127, 205, 283, 361, 439, 1352, 1429, 1506, 1583, 1660, 1737, 1814, 1891, 1968, 2045, 2122
22	9181	9214	463434	463467	68	97	82	51	994549-994551, 1040566-1040567	131, 209, 287, 1201, 1278
23	9472	9513	463725	463766	79	91	84	25	994559-994561, 1055024-1055036	288, 366, 444, 3126-3127, 3195-3197, 3265-3266, 3335-3336, 3404-3405, 3475-3476
24	9667	9730	463920	463983	75	94	86	35	994562-994564, 1040612-1040613	55, 522, 600, 2280, 2357
25	10095	10121	464348	464374	66	95	84	13	994571, 1055043-1055048	601, 3129, 3199, 3268, 3339, 3407, 3408
26	10133	10158	464386	464411	84	92	88	n.d.	994572-994574, 1040633	56,134, 212, 1434
27	10237	10277	464490	464530	72	90	82	n.d.	994579-994580, 1040653-1040658	57, 602, 665, 742, 819, 896, 2974, 3051
28	10311	10353	464564	464606	80	95	89	n.d.	994581-994583, 1040663-1040666	135, 213, 291, 1281, 1358, 1435, 1512
29	N/A	N/A	439072	439126	69	99	87	47	994809-994811, 1041407-1041414, 1364281, 1365254-1365255, 1365278, 1365281, 1394526	475, 553, 631, 1920, 1997, 2074, 2151, 2228, 2305, 2382, 2459, 3625-3626, 3642-3643
30	N/A	N/A	17722	17748	72	99	87	n.d.	994605, 1055065-1055071	138, 3134, 3202-3203, 3270, 3343, 3412, 3480
31	N/A	N/A	85512	85545	64	92	76	n.d.	994630, 1055084-1055094	219, 3137, 3206-3207, 3273-3274, 3346-3347, 3415-3416, 3483-3484

32	N/A	N/A	179779	179809	43	96	81	n.d.	994690, 1055106-1055113	538, 3140, 3210, 3276-3277, 3350, 3419-3420, 3487
33	N/A	N/A	184181	184213	85	99	94	n.d.	994693, 1055123-1055132	149, 3143, 3212-3213, 3280, 3352-3353, 3422-3423, 3490-3491
34	N/A	N/A	203033	203066	48	94	76	n.d.	994700, 1055137-1055147	72, 3144-3145, 3214-3215, 3282-3283, 3355-3356, 3425, 3493-3494
35	N/A	N/A	203889	203914	81	98	92	n.d.	994701, 1055151-1055156	150, 3147, 3285, 3357-3358, 3426, 3495
36	N/A	N/A	210720	210755	47	96	80	n.d.	994702, 1055157-1055168	228, 3148-3149, 3217-3218, 3286-3287, 3359-3360, 3427-3429, 3496
37	N/A	N/A	212027	212056	69	90	80	n.d.	994703, 1055174-1055182	306, 3151-3152, 3220-3221, 3362, 3430-3431, 3498-3499
38	N/A	N/A	217274	217309	40	97	73	n.d.	994706, 1055186-1055197	540, 3153, 3222-3223, 3290-3291, 3364-3365, 3433-3434, 3500-3502
39	N/A	N/A	226995	227019	75	90	81	n.d.	994713, 1055208-1055212	463, 3156, 3226, 3294, 3368, 3436
40	N/A	N/A	251500	251533	68	94	83	n.d.	994717, 1055224-1055234	152, 3159-3160, 3229, 3297-3298, 3370-3371, 3439-3440, 3506-3507
41	N/A	N/A	284223	284260	96	99	98	n.d.	994731, 1055240-1055252	621, 3162, 3163, 3231, 3232, 3299, 3300, 3374, 3375, 3442, 3443, 3509, 3510
42	N/A	N/A	284331	284370	39	98	88	n.d.	994732, 1055253-1055266	76, 3164-3166, 3233-3234, 3301-3302, 3376-

										3377, 3444-3446, 3511-3512
43	N/A	N/A	291004	291043	93	99	97	n.d.	994734, 1055268-1055281	232, 3167-3168, 3236-3237, 3303-3305, 3378-3379, 3447-3449, 3513-3514
44	N/A	N/A	296997	297034	73	99	95	n.d.	994735, 1055283-1055295	310, 3169-3170, 3238-3240, 3306-3307, 3380-3381, 3450-3451, 3516-3517
45	N/A	N/A	306737	306769	78	98	92	n.d.	994740, 1055300-1055305	77, 3171, 3241, 3309, 3383, 3453, 3519
46	N/A	N/A	318484	318519	88	99	96	n.d.	994743, 1041154, 1055310-1055317	311, 2143, 3173-3174, 3243, 3311, 3385, 3454-3455, 3520
47	N/A	N/A	332352	332391	54	99	90	n.d.	994756, 1055321-1055334	79, 3175-3177, 3245-3246, 3313-3314, 3387-3388, 3456-3458, 3521-3522
48	N/A	N/A	347813	347852	57	99	84	n.d.	994761, 1055337-1055350	469, 3178-3179, 3248-3249, 3316-3317, 3389-3391, 3459-3460, 3523-3525
49	N/A	N/A	437786	437815	74	97	91	12	1041316-1041322	2302, 2379, 2456, 2533, 2610, 2687, 2764
50	N/A	N/A	439429	439463	81	96	87	14	1041438-1041443, 1342051, 1342058, 1342043, 1342040	1844, 1921, 1998, 2075, 2152, 2229, 3547, 3572
51	N/A	N/A	442680	442711	78	93	87	30	1041636-1041639	2312, 2389, 2466, 2543
52	N/A	N/A	446727	446761	74	93	84	n.d.	1041936-1041941	782, 859, 936, 1013, 1090, 1167
53	N/A	N/A	446925	446970	59	91	77	n.d.	994871-994873, 1041961-1041966	327, 405, 483, 2707, 2784, 2861, 2938, 3015, 3092

54	N/A	N/A	451523	451560	82	95	89	n.d.	1042239-1042244	1946, 2023, 2100, 2177, 2254, 2331
55	N/A	N/A	451681	451718	72	91	83	0	1042253-1042258	715, 792, 869, 946, 3024, 3101
6	99	140	2609	2650	43	90	76	n.d.	994310-994313, 1054946-1054957	179, 257, 335, 413, 3111-3113, 3183, 3253-3254, 3321-3322, 3394-3395, 3464-3465

*Only a single compound tested *in vitro*; see *in vivo* column for average % reduction.

Nonlimiting disclosure and incorporation by reference

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

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

Although the sequence listing accompanying this filing identifies each sequence as either "RNA" or "DNA" as required, in reality, those sequences may be modified with any combination of chemical modifications. One of skill in the art will readily appreciate that such designation as "RNA" or "DNA" to describe modified oligonucleotides is, in certain instances, arbitrary. For example, an oligonucleotide comprising a nucleoside comprising a 2'-OH sugar moiety and a thymine base could be described as a DNA having a modified sugar (2'-OH in place of one 2'-H of DNA) or as an RNA having a modified base (thymine (methylated uracil) in place of an uracil of RNA). Accordingly, nucleic acid sequences provided herein, including, but not limited to those in the sequence listing, are intended to encompass nucleic acids containing any combination of natural or modified RNA and/or DNA, including, but not limited to such nucleic acids having modified nucleobases. By way of further example and without limitation, an oligomeric compound having the nucleobase sequence "ATCGATCG" encompasses any oligomeric compounds having such nucleobase sequence, whether modified or unmodified, including, but not limited to, such compounds comprising RNA bases, such as those having sequence "AUCGAUCG" and those having some DNA bases and some RNA bases such as "AUCGATCG" and oligomeric compounds having other modified nucleobases, such as "AT^{m}CGAUCG," wherein ^{m}C indicates a cytosine base comprising a methyl group at the 5-position.

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

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

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 salt thereof" expressly includes all such forms that may be fully or partially protonated/de-protonated/in association with a cation. In certain instances, one or more specific cation is identified. In certain embodiments, modified oligonucleotides 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. For example, 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 Na+ ions. However, the mass of the protons are nevertheless counted toward the weight of the dose, and the mass of the Na+ ions are not counted toward the weight of the dose. Thus, for example, a dose, or dosage unit, of 10 mg of Compound No. 1371311, equals the number of fully protonated molecules that weighs 10 mg. This would be equivalent to 10.59 mg of solvent-free, sodium acetate-free, anhydrous sodiated Compound No. 1371311. When an oligomeric compound comprises a conjugate group, the mass of the conjugate group is 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.

EXAMPLES

Example 1: Effect of 5-10-5 MOE gapmer modified oligonucleotides on human ATXN1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to human ATXN1 nucleic acid were designed and tested for their single dose effects on ATXN1 mRNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had similar culture conditions.

The modified oligonucleotides in the tables below are 5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides and the 3' and 5' wings each consist of five 2'-MOE modified nucleosides. The motif for the gapmers is (from 5' to 3'): eeeeeddddddddddeeeee; wherein "d" represents a 2'-β-D-deoxyribosyl sugar, and 'e' represents a 2'-MOE modified ribosyl sugar. The internucleoside linkage motif for the gapmers is (from 5' to 3'): sooossssssssssooss; wherein 'o' represents a phosphodiester internucleoside linkage and 's' represents a phosphorothioate internucleoside linkage. Each cytosine residue is a 5-methyl cytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. Each modified oligonucleotide listed in the Tables below is 100% complementary to SEQ ID NO: 1 (GENBANK Accession No. NM_000332.3), or SEQ ID NO: 2 (the complement of GENBANK Accession No. NC_000006.12 truncated from nucleotides 16296001 to 16764000). 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular gene sequence.

Cultured A-431 cells were treated with modified oligonucleotide at a concentration of 4,000nM by free uptake at a density of 10,000 cells per well for a treatment period of 48 hours. At the end of their treatment period, total RNA was isolated from the cells and ATXN1 RNA levels were measured by quantitative real-time RTPCR. ATXN1 RNA levels were measured by Human ATXN1 primer probe set RTS37573 (forward sequence CATCCAGAGTGCAGAGATAAGC, designated herein as SEQ ID NO: 11; reverse sequence ACTCTACCAAAACTTCAACGCT, designated herein as SEQ ID NO: 12; probe sequence AGAGGATTGAAGACAGCCATAGCCC, designated herein as SEQ ID NO: 13). ATXN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Results are presented in the tables below as percent ATXN1 RNA levels relative to untreated control cells (%control). Each table represents results from an individual assay plate. The Compound No. marked with an asterisk (*) indicates 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 2

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994308	6	25	2516	2535	CTGCGGTATACTCTGCTCTC	96	23
994316	305	324	10716	10735	GGAGGAGGAGATTGCTGTAC	13	24

994324	435	454	106177	106196	GTGCAGGCTGAAATCCACTC	32	25
994332	691	710	277909	277928	GTGTTCTTTCTTCCTTTCAC	37	26
994340	959	978	435678	435697	ATTTCATTTTTCGCCGTCCC	53	27
994348	1190	1209	435909	435928	CTTTGTGTAAACCTATTCCC	29	28
994356	1881	1900	436600	436619	TCAGCTTTCTTGGTGGCCTC	103	29
994364	2264	2283	436983	437002	GTGTGGTCTGAATGACCGTG	76	30
994372	2728	2747	437447	437466	GTCTTCCACCTTCTTTAGCT	65	31
994380*	2816	2835	437535	437554	GGCTGTCTTCAATCCTCTCT	4	32
994388	3139	3158	457392	457411	TCCGTTTTCCTGCTCGGCAT	32	33
994396	3398	3417	457651	457670	ACTTGCCTACATTAGACCGG	30	34
994404	3630	3649	457883	457902	ACCGCTCCTGCTGTGCCCTT	35	35
994412	4246	4265	458499	458518	CGCTCTCTCCCTCTCCCCCA	55	36
994420	4617	4636	458870	458889	TGTTTTTGTTTTTTCCCCAA	2	37
994428	4708	4727	458961	458980	ATTGAAACTTTCAATATCTT	50	38
994436	4858	4877	459111	459130	CCCTTTTCTCTCAGTTTCTC	37	39
994444	5428	5447	459681	459700	TTTTTTTTAAAGCACTTTAA	73	40
994452	5560	5579	459813	459832	GATTTTTTTTTTAATTTGTG	72	41
994460	5980	5999	460233	460252	TGTGTGTTTTTCTGAGTCCA	4	42
994468	6050	6069	460303	460322	GTGTTTTCCCATCTTAGTGT	7	43
994476	6324	6343	460577	460596	TGGGAGGCTCTCTCCCTCCT	86	44
994484	6937	6956	461190	461209	CGGTAAATATTGCAAAGTGG	4	45
994492	7083	7102	461336	461355	GTTTGTTGGTTTCTTATTAA	5	46
994500	7217	7236	461470	461489	GGCATCCATCTCTGTATCCC	34	47
994508	7868	7887	462121	462140	CATTGGAGATTTTTCTCTCT	17	48
994516	8196	8215	462449	462468	TCTCTATTTCAGAAATTCTG	34	49
994524	8379	8398	462632	462651	ATCTATGTAAAAGAAATCTC	58	50
994532	8542	8561	462795	462814	AATTTTTTAAAACATTACCT	57	51
994540	8764	8783	463017	463036	GGTATAGTTTAAGAGCCTTT	10	52
994548	9176	9195	463429	463448	GCCTCTTTATATTAAATAAA	76	53
994556	9296	9315	463549	463568	TCTGAATTTAAGAATTGTAA	52	54
994564	9707	9726	463960	463979	ACCTAATACTTGGTATTCTG	17	55
994572	10133	10152	464386	464405	GTGTCTGTTTTCCCTTGGCC	9	56
994580	10241	10260	464494	464513	GTATGCACTTAAAATTTTCT	11	57
994588	10381	10400	464634	464653	ATAGAATATGAATTCTTCCA	30	58
994596	10613	10632	464866	464885	ATTGGCACTGTTATTTTATT	48	59
994604	N/A	N/A	15633	15652	GGCTCTTTAAATATTACTCC	63	60
994612	N/A	N/A	31191	31210	GTTTGACTAGATGTGCTTCT	7	61
994620	N/A	N/A	41645	41664	TCTTGAGCTTTTAATTTTAC	22	62
994628	N/A	N/A	72785	72804	TGCTCCTTTTATCATTGTCA	16	63
994636	N/A	N/A	94229	94248	CGGTGGTTTGTTGTACCCTT	62	64
994644	N/A	N/A	111441	111460	TGTACTCTATAATTTTTTAA	82	65
994652	N/A	N/A	134750	134769	TGAGCTGCTTTTCATATTCT	28	66
994660	N/A	N/A	148412	148431	CAATAGACAAAAATTATCAT	78	67
			149523	149542			
994668	N/A	N/A	148748	148767	TTTCCGAAGCTGCTATATGT	63	68

			149859	149878			
994676	N/A	N/A	155724	155743	GTCTCTCTTTTTCTAAGTCA	46	69
994684	N/A	N/A	169830	169849	AGACTAATATATATATATAT	52	70
			170088	170107			
994692	N/A	N/A	180504	180523	GGGTCTCTTCATCTACCTTC	61	71
994700	N/A	N/A	203037	203056	TGTTCCTTTCTTCTTTGTTC	21	72
994708	N/A	N/A	219463	219482	GGGTGTGTATTCAATTCTCT	59	73
994716	N/A	N/A	250181	250200	GTGACTTTAAAGCTTTCCTG	53	74
994724	N/A	N/A	269848	269867	ACTGAGAGGCATCTCCAGTG	86	75
			269877	269896			
994732	N/A	N/A	284341	284360	TGTCAACTAGTTCTTATCAC	7	76
994740	N/A	N/A	306740	306759	GGTAAGGGCCACTAAATCTG	5	77
			306826	306845			
994748	N/A	N/A	322467	322486	CTTACCACAGAGACATGCCC	56	78
			323729	323748			
994756	N/A	N/A	332362	332381	GGAGTATTATAACAATTTGC	5	79
994764	N/A	N/A	354092	354111	GTCTGGGCTGATGATGCTGG	16	80
994772	N/A	N/A	369873	369892	GTCTGCCTTTAACATTTTTC	25	81
994780	N/A	N/A	386759	386778	TGTTGTTTATAAGTTTACGG	12	82
994788	N/A	N/A	406846	406865	TGCAGCTTATTTTATAGGTG	8	83
994796	N/A	N/A	422947	422966	CGGTGTCTTAATATCCTCAG	32	84
994804	N/A	N/A	437891	437910	GTTCCTCATCTTAATCACAG	24	85
994812	N/A	N/A	439175	439194	GTGACTCATCTTGGCTACAG	32	86
994820	N/A	N/A	440213	440232	ATTTTCCATGTGTCACCTGG	34	87
994828	N/A	N/A	441396	441415	GTGCAGTGTCAGCAGTGCCT	44	88
994836	N/A	N/A	443271	443290	GTTGTCTTACTGATCTGGAG	12	89
994844	N/A	N/A	444292	444311	TGAGACCTCTCTCTACTTGC	43	90
994852	N/A	N/A	445329	445348	TCAGTCCTTGGTGGAAGTGT	50	91
994860	N/A	N/A	445809	445828	TCTGTTGTTTAAATATGTCT	49	92
994868	N/A	N/A	446320	446339	TCTTTCATCTCTGGATGCCC	42	93
994876	N/A	N/A	447587	447606	GTGTTCTATCTCCAGAGTCT	20	94
994884	N/A	N/A	448144	448163	TGGTGAAGATAATGATGATC	28	95
994892	N/A	N/A	449029	449048	TCCAGTTTTAATAAAAGTTC	61	96
994900	N/A	N/A	451116	451135	ATTTTACTTAATTTTTACAA	77	97
994908	N/A	N/A	452370	452389	ATGTGCATATATACATAGAC	23	98
994916	N/A	N/A	453097	453116	CTTTTCTACTTCATCTTCTT	61	99
994924	N/A	N/A	455432	455451	GTGTTCTCTGGTGAGCCCCA	59	100

Table 3

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994309	23	42	2533	2552	TGTAGTAGAAATGATGTCTG	75	101

994317	368	387	106110	106129	AAATAGACTCTTTCACTATG	41	102
994325	500	519	178110	178129	GTGGCAGTGGAGAATCTCAG	10	103
994333	761	780	277979	277998	TCAGCCTATACTTCACCATG	40	104
994341	965	984	435684	435703	GGTTGGATTTCATTTTTCGC	17	105
994349	1363	1382	436082	436101	TCCACTGTATTGGGAGGACC	73	106
994357	1882	1901	436601	436620	CTCAGCTTTCTTGGTGGCCT	93	107
994365	2455	2474	437174	437193	CGCTTCCATGTCAGTGCTGC	62	108
994373	2739	2758	437458	437477	TCTGTTTTTAAGTCTTCCAC	35	109
994381*	2848	2867	437567	437586	GGCGAACTGTATCACGGCCA	49	110
994389	3147	3166	457400	457419	TGGTTGATTCCGTTTTCCTG	63	111
994397	3467	3486	457720	457739	CCTACAGTACAGTAATCTGG	32	112
994405	3750	3769	458003	458022	CACGGGACTTTTCTCCTGAC	49	113
994413	4249	4268	458502	458521	GTTCGCTCTCTCCCTCTCCC	13	114
994421	4618	4637	458871	458890	TTGTTTTTGTTTTTTCCCCA	1	115
994429	4759	4778	459012	459031	CATTTATTGTCACATACTAG	19	116
994437	4922	4941	459175	459194	GGTTCTTTAAAAGTTCATCT	2	117
994445	5429	5448	459682	459701	CTTTTTTTTAAAGCACTTTA	37	118
994453	5571	5590	459824	459843	GGTTGATACCAGATTTTTTT	19	119
994461	5981	6000	460234	460253	GTGTGTGTTTTTCTGAGTCC	6	120
994469	6054	6073	460307	460326	ATGTGTGTTTTCCCATCTTA	8	121
994477	6421	6440	460674	460693	GTCTCCTTGGCTGGCTCTTT	21	122
994485	7018	7037	461271	461290	GTGTTCCATTGTAAACGCAA	36	123
994493	7087	7106	461340	461359	TCTTGTTTGTTGGTTTCTTA	3	124
994501	7243	7262	461496	461515	TCCACTTTAAAAGATCTGAG	18	125
994509	7892	7911	462145	462164	GCACGGTATTAGTGTCTTCA	6	126
994517	8204	8223	462457	462476	TCTTAAATTCTCTATTTCAG	34	127
994525	8487	8506	462740	462759	TCTTCAGCTTCTCAAATCAG	46	128
994533	8648	8667	462901	462920	TCTGCTTTTTTTTTTTTACA	45	129
994541	8867	8886	463120	463139	AAGTACTTTCAGCATAGGAA	13	130
994549	9189	9208	463442	463461	CGTATTTATTCTGGCCTCTT	14	131
994557	9428	9447	463681	463700	AATACAGTTGAACCATTTGT	28	132
994565	9725	9744	463978	463997	ACAGCTTGAGCTAGTGTCAC	32	133
994573	10135	10154	464388	464407	TGGTGTCTGTTTTCCCTTGG	16	134
994581	10311	10330	464564	464583	GGAATTACAGAGAGTATGCA	11	135
994589	10506	10525	464759	464778	GTTTTATTATAATAATGAAA	76	136
994597	198	217	9914	9933	GTAGTAGTTTTTGTGAGGTA	14	137
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	6	138
994613	N/A	N/A	33070	33089	ATTTTGACTTTTGATTGGTG	12	139
994621	N/A	N/A	44962	44981	GGGACTCTGTCTTTATTTCC	75	140
			44984	45003			
994629	N/A	N/A	77141	77160	ATGTTTCTATCTAAGTCCCA	40	141
994637	N/A	N/A	98148	98167	GTGTGCATTTTTAATTTTGT	55	142
994645	N/A	N/A	112180	112199	TGAGGACATCATGATGGTGC	20	143
994653	N/A	N/A	139451	139470	GTTTTGTTTCAGTATTAGGT	3	144
994661	N/A	N/A	148441	148460	TACATCCTGAAAATCACAGC	42	145

			149552	149571			
994669	N/A	N/A	148797	148816	CTCTCACTTTTCTTCTCCTT	59	146
			149908	149927			
994677	N/A	N/A	157700	157719	GTCTCCTTACATAGTGCTGC	42	147
994685	N/A	N/A	169837	169856	ATATATTAGACTAATATATA	86	148
			169922	169941			
994693	N/A	N/A	184184	184203	TCAGGTTTATATGTATACAA	7	149
994701	N/A	N/A	203893	203912	GTTTGTTTAGATTTATCCTC	5	150
994709	N/A	N/A	219913	219932	GTCATAGCTCTCCTCTGCAC	46	151
994717	N/A	N/A	251504	251523	GTCAGCATACTTAGCTTTTC	16	152
994725	N/A	N/A	269857	269876	CAGGGCTGGACTGAGAGGCA	58	153
			269886	269905			
994733	N/A	N/A	288893	288912	TGAGACTATTATAGTTTCCA	12	154
994741	N/A	N/A	308086	308105	TAAAATGCACCAATCAACGC	38	155
			308110	308129			
994749	N/A	N/A	328172	328191	GTTACTTTATTTCTCTAGGG	10	156
994757	N/A	N/A	333463	333482	ATTTGTCTTGTTGTATGTTG	15	157
994765	N/A	N/A	355633	355652	GTTATTTTAAATAGTGGCCT	65	158
994773	N/A	N/A	369913	369932	TCTTTGGCTTTTAGACCTGT	35	159
994781	N/A	N/A	390011	390030	ATGTTATATCAATGTTCTGT	6	160
994789	N/A	N/A	413612	413631	GTCTCAGCTCAAGAGTCTGT	75	161
994797	N/A	N/A	430371	430390	TGGCCTGTATATCTATGGAC	75	162
994805	N/A	N/A	438153	438172	TCAGCCATAGCTCACTACAG	26	163
994813	N/A	N/A	439396	439415	GTCCCATTTGAATGTTTTCA	15	164
994821	N/A	N/A	440225	440244	TCACTCATGTTTATTTTCCA	58	165
994829	N/A	N/A	441413	441432	TCTGAATTTCTCTGTGGGTG	11	166
994837	N/A	N/A	443454	443473	TGTACTCTTCAGAGAAGCTG	64	167
994845	N/A	N/A	444302	444321	GTTAGGTGTGTGAGACCTCT	61	168
994853	N/A	N/A	445380	445399	TCTGTGAGTGTTCTATTTAA	27	169
994861	N/A	N/A	445876	445895	TGGTGCTATGTCTATATACA	25	170
994869	N/A	N/A	446356	446375	TGGCCTTTATACTTTTGTAA	92	171
994877	N/A	N/A	447624	447643	TGTATATTTGTCTGTTTTGC	9	172
994885	N/A	N/A	448318	448337	CTTCCTTTTTTTATTTTGAG	17	173
994893	N/A	N/A	449699	449718	TCTTTATTTTATAATTAGGT	63	174
994901	N/A	N/A	451209	451228	TCTATGGTCCTCAGTCTCCT	57	175
994909	N/A	N/A	452421	452440	GTGACACTATTTGGTTTCAA	59	176
994917	N/A	N/A	453098	453117	GCTTTTCTACTTCATCTTCT	59	177
994925	N/A	N/A	455497	455516	TGGGCTTTTGATAGTGTTAA	20	178

Table 4

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994310	99	118	2609	2628	GTTGCTCTGGCTGCTGCTCC	23	179
994318	413	432	106155	106174	TCTCTCTTGTTCCTGGTCTG	9	180
994326	515	534	178125	178144	GCTTGAGTAGAAAGGGTGGC	40	181
994334	879	898	435598	435617	GTCACATTTGATTTCTGTAG	12	182
994342	966	985	435685	435704	TGGTTGGATTTCATTTTTCG	24	183
994350	1550	1569	436269	436288	GCTGCTGCTGCTCAGCCTTG	62	184
994358	1889	1908	436608	436627	GGCTGCTCTCAGCTTTCTTG	89	185
994366	2554	2573	437273	437292	GTTGAAGTTCTCGCTCTTGG	23	186
994374	2740	2759	437459	437478	TTCTGTTTTTAAGTCTTCCA	30	187
994382*	2849	2868	437568	437587	CGGCGAACTGTATCACGGCC	30	188
994390	3154	3173	457407	457426	ACTCCCCTGGTTGATTCCGT	54	189
994398	3481	3500	457734	457753	CTGTGTTATTTTAGCCTACA	5	190
994406	3932	3951	458185	458204	GTTCCTGATGTTGATTTTGC	27	191
994414	4251	4270	458504	458523	GTGTTCGCTCTCTCCCTCTC	24	192
994422	4621	4640	458874	458893	TTTTTGTTTTTGTTTTTTCC	14	193
994430	4762	4781	459015	459034	GGTCATTTATTGTCACATAC	2	194
994438	4971	4990	459224	459243	ACTGCAGGAATATCACACAA	54	195
994446	5485	5504	459738	459757	GTTTAGTTGCAGCCATCCAA	8	196
994454	5572	5591	459825	459844	GGGTTGATACCAGATTTTTT	29	197
994462	5983	6002	460236	460255	TGGTGTGTGTTTTTCTGAGT	7	198
994470	6121	6140	460374	460393	ATTTTATAATTCCTATACCT	74	199
994478	6470	6489	460723	460742	CATTCACTATTCCGTGTGGT	41	200
994486	7024	7043	461277	461296	GTGATTGTGTTCCATTGTAA	5	201
994494	7088	7107	461341	461360	TTCTTGTTTGTTGGTTTCTT	5	202
994502	7384	7403	461637	461656	TCACAATTCCAAGTTAGAAA	16	203
994510	7930	7949	462183	462202	GTACCGAGAGCTCTGCTTCC	54	204
994518	8208	8227	462461	462480	GTGTTCTTAAATTCTCTATT	3	205
994526	8492	8511	462745	462764	TGTTTTCTTCAGCTTCTCAA	18	206
994534	8649	8668	462902	462921	CTCTGCTTTTTTTTTTTTAC	45	207
994542	8893	8912	463146	463165	GTTTAGACTAAGAAGGGAGC	22	208
994550	9191	9210	463444	463463	TCCGTATTTATTCTGGCCTC	32	209
994558	9462	9481	463715	463734	AGATACTACCTATTGGCCAA	63	210
994566	9758	9777	464011	464030	GCACCGAGCTTCTTGGTAAC	60	211
994574	10139	10158	464392	464411	GTTCTGGTGTCTGTTTTCCC	8	212
994582	10328	10347	464581	464600	GTACAATATTTTACACTGGA	5	213
994590	10548	10567	464801	464820	ATTTATTTAAAACAATTTTG	86	214
994598	201	220	9917	9936	CTTGTAGTAGTTTTTGTGAG	36	215
994606	N/A	N/A	18215	18234	GGAGGGTGCTTAGTCCTTCC	69	216
			18273	18292			

994614	N/A	N/A	34101	34120	GTTTGGCACACAGTAGGTGC	29	217
			355035	355054			
994622	N/A	N/A	46490	46509	GTGACTGCTGCTGATACCTG	39	218
994630	N/A	N/A	85516	85535	GTTTGATATGCTATGCTCAC	26	219
994638	N/A	N/A	98883	98902	TGTTTGGTTGAAGTATGTGG	30	220
994646	N/A	N/A	115266	115285	ATGTGGGTATTTAATGTTTC	17	221
994654	N/A	N/A	140695	140714	GTCTTTCTAAATGGTTGTAC	31	222
994662	N/A	N/A	148489	148508	TTCAGCATGATCTCAGTTCT	25	223
			149600	149619			
994670	N/A	N/A	148889	148908	ATGACATAATTCTAATAACT	58	224
			150000	150019			
994678	N/A	N/A	159922	159941	TCTCCTTATCTTGTCCTCTC	47	225
994686	N/A	N/A	169926	169945	TATTATATATTAGACTAATA	81	226
			170006	170025			
994694	N/A	N/A	185906	185925	GTTCTATTTTATAATAGTAG	70	227
994702	N/A	N/A	210730	210749	TGTGTAATACTCCATTTTTC	18	228
994710	N/A	N/A	223261	223280	GTTTGTGTTGTGTTTTACAG	19	229
994718	N/A	N/A	251771	251790	GTTTTCATACACAGTTCTTC	23	230
994726	N/A	N/A	270287	270306	ATTATATTACATTATACTTG	100	231
994734	N/A	N/A	291014	291033	TCCTGGGTTTTTAGTTTTCC	4	232
994742	N/A	N/A	310465	310484	TGAGGATTACATCAGTGTAA	4	233
994750	N/A	N/A	328842	328861	TCTTGGGTAGATGAGGTTTG	11	234
994758	N/A	N/A	337233	337252	TCTTGTTTTTTCCTTTCTTG	25	235
994766	N/A	N/A	357070	357089	GTCTCCTTTGTTCCGTGTAC	21	236
994774	N/A	N/A	372154	372173	GTCTTTTTATTTCTCTGCCC	11	237
994782	N/A	N/A	396255	396274	TTGCAAGAAGGTATGCCTAG	61	238
			396277	396296			
994790	N/A	N/A	413815	413834	TCCTGTTTACAACAAAGCTC	66	239
994798	N/A	N/A	430661	430680	TCTTTCTTTGCTATAATTTC	84	240
994806	N/A	N/A	438267	438286	GTCTGCTGATCTATCTGTTG	20	241
994814	N/A	N/A	439492	439511	ATTAGTTTATCTTTTTTTTC	78	242
994822	N/A	N/A	440914	440933	CTGTCAGTAGAGAGATTTAG	41	243
994830	N/A	N/A	441421	441440	TGCACATTTCTGAATTTCTC	13	244
994838	N/A	N/A	443819	443838	GTACCAGCTAATCCATTCAA	43	245
994846	N/A	N/A	444486	444505	TGTTCTGTATAATAATGTAA	60	246
994854	N/A	N/A	445456	445475	CGAGAGACCCATTTACTGCA	16	247
994862	N/A	N/A	446068	446087	TGGGCTCATAATTATTTTTT	71	248
994870	N/A	N/A	446878	446897	AAGTCATTTTATGATCTTGC	55	249
994878	N/A	N/A	447631	447650	ATTTACTTGTATATTTGTCT	12	250
994886	N/A	N/A	448328	448347	GTTTCCATAGCTTCCTTTTT	37	251
994894	N/A	N/A	449737	449756	TCTCAAATAGGTACACTCAA	40	252
994902	N/A	N/A	451578	451597	TTTTGTTTAAAGGGTTTTAC	85	253
994910	N/A	N/A	452423	452442	GTGTGACACTATTTGGTTTC	49	254
994918	N/A	N/A	453104	453123	ATTGTTGCTTTTCTACTTCA	73	255
994926	N/A	N/A	455500	455519	AAGTGGGCTTTTGATAGTGT	20	256

Table 5

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994311	103	122	2613	2632	TGCTGTTGCTCTGGCTGCTG	62	257
994319	417	436	106159	106178	TCTTTCTCTCTTGTTCCTGG	5	258
994327	533	552	178143	178162	TCTTTTCACGAAGATTTTGC	22	259
994335	881	900	435600	435619	AAGTCACATTTGATTTCTGT	31	260
994343	969	988	435688	435707	TCTTGGTTGGATTTCATTTT	31	261
994351	1634	1653	436353	436372	TGAGGTGCTGCTGCTGCTGC	15	262
994359	1904	1923	436623	436642	TGGCCTGCTGCAGCCGGCTG	82	263
994367	2555	2574	437274	437293	GGTTGAAGTTCTCGCTCTTG	14	264
994375	2742	2761	437461	437480	TCTTCTGTTTTTAAGTCTTC	30	265
994383	2952	2971	457205	457224	TGGCTGGTTCTCTCCGGACA	71	266
994391	3245	3264	457498	457517	TGCTGGGTTCTATTTTGGTG	38	267
994399	3490	3509	457743	457762	ATGTAAATACTGTGTTATTT	32	268
994407	3933	3952	458186	458205	GGTTCCTGATGTTGATTTTG	33	269
994415	4254	4273	458507	458526	TGGGTGTTCGCTCTCTCCCT	37	270
994423	4636	4655	458889	458908	AAAGCAACTTAGTTTTTTTT	46	271
994431	4774	4793	459027	459046	GTAGTACTTGGTGGTCATTT	67	272
994439	5033	5052	459286	459305	TGCTACATTTATTTATGCTC	36	273
994447	5491	5510	459744	459763	TGTTCAGTTTAGTTGCAGCC	4	274
994455	5593	5612	459846	459865	AATACTAGACAGCCAAAATG	34	275
994463	5986	6005	460239	460258	AGGTGGTGTGTGTTTTTCTG	4	276
994471	6124	6143	460377	460396	ATTATTTTATAATTCCTATA	79	277
994479	6535	6554	460788	460807	TCCAGGCTACATGGCTCCAG	27	278
994487	7056	7075	461309	461328	ATTTTTTTCTTTTCGCCCTG	21	279
994495	7091	7110	461344	461363	AGGTTCTTGTTTGTTGGTTT	2	280
994503	7392	7411	461645	461664	ATAGAGGCTCACAATTCCAA	12	281
994511	8000	8019	462253	462272	TGTTGAGCTGCTTGTGGTTC	63	282
994519	8212	8231	462465	462484	TGATGTGTTCTTAAATTCTC	24	283
994527	8495	8514	462748	462767	TTTTGTTTTCTTCAGCTTCT	19	284
994535	8651	8670	462904	462923	TTCTCTGCTTTTTTTTTTTT	44	285
994543	8984	9003	463237	463256	CAAGATTATATTCTTTGGGT	11	286
994551	9194	9213	463447	463466	TGCTCCGTATTTATTCTGGC	3	287
994559	9472	9491	463725	463744	GTTATTGTATAGATACTACC	17	288
994567	9841	9860	464094	464113	GCACTAACTAAAGGATTTAC	14	289
994575	10146	10165	464399	464418	AACCCAAGTTCTGGTGTCTG	32	290
994583	10334	10353	464587	464606	GTGCAAGTACAATATTTTAC	5	291
994591	10601	10620	464854	464873	ATTTTATTAGTACGAGTATA	41	292
994599	204	223	9920	9939	GTGCTTGTAGTAGTTTTTGT	30	293
994607	N/A	N/A	18221	18240	GTTAGTGGAGGGTGCTTAGT	24	294

			18279	18298			
994615	N/A	N/A	39140	39159	TCCTGTTATTTTGGTACTGG	24	295
994623	N/A	N/A	47154	47173	GTTTGCCTACTCCTGGTCTG	28	296
994631	N/A	N/A	85766	85785	GTTGACTATCTTATTTTTTC	20	297
994639	N/A	N/A	99612	99631	TCTTGCTTTTAATTTTTTTG	37	298
994647	N/A	N/A	117178	117197	GTTCACCTACATGTTTCCCC	16	299
994655	N/A	N/A	144856	144875	TCTTTTTTTTTTAATTACAG	79	300
994663	N/A	N/A	148529	148548	TGGTGCACTCAGCTCTACCT	62	301
			149640	149659			
994671	N/A	N/A	148965	148984	AAAAATCCTGATCAAAAAAA	76	302
			150076	150095			
994679	N/A	N/A	160587	160606	GGCTCCATACTCCATTCTGT	40	303
994687	N/A	N/A	170194	170213	TGTATAATATTCCATTCTGT	48	304
994695	N/A	N/A	185938	185957	ATTTTATTACATTTTTCTTG	77	305
994703	N/A	N/A	212031	212050	TCTATGTTAGTCATTTCTCT	98	306
994711	N/A	N/A	223958	223977	TCTTGACATGATGTTTCCCT	60	307
994719	N/A	N/A	256280	256299	ATTACCTTAAAACTACCTTG	54	308
994727	N/A	N/A	271835	271854	TAAGCCATGCCTGGACTTCG	55	309
			271877	271896			
994735	N/A	N/A	297005	297024	GTTTGCATTAAATGACTGTG	2	310
994743	N/A	N/A	318485	318504	TGTTTGATATTTCTTTTTTT	10	311
994751	N/A	N/A	328883	328902	TCTTGGGTAACTAGATGATG	15	312
994759	N/A	N/A	341935	341954	GTTTTTTTTTTTATTTGCCT	4	313
994767	N/A	N/A	357089	357108	GTCAGGTTATAATGACCCTG	49	314
994775	N/A	N/A	376249	376268	TCTTCTGTATTTAATTCTTC	11	315
994783	N/A	N/A	396693	396712	GTTATTGTGTTTATATTCAG	10	316
994791	N/A	N/A	414662	414681	TGGTGACATCTTGTTTCTAC	15	317
994799	N/A	N/A	433785	433804	TGAGCCACTGTGTGTAGCCA	52	318
994807	N/A	N/A	438269	438288	TTGTCTGCTGATCTATCTGT	25	319
994815	N/A	N/A	439696	439715	GTTTTTTATTTTTAAATTAG	62	320
994823	N/A	N/A	441090	441109	CCTTGCACTTTTGTTTCTAC	7	321
994831	N/A	N/A	442195	442214	TCAGTACATGTTCATCTTAA	10	322
994839	N/A	N/A	443918	443937	CGGCATGTTCAATGTTGGCA	14	323
994847	N/A	N/A	444822	444841	GTGAGCTATTATGGTGTCAC	101	324
994855	N/A	N/A	445546	445565	GTCTGCTTTCCTGGAAGGCT	37	325
994863	N/A	N/A	446159	446178	ATCCCCCTAAATCGACTCCT	63	326
994871	N/A	N/A	446925	446944	GTTATTTTCTCTCCACTCTC	33	327
994879	N/A	N/A	447641	447660	ATTCTTTTTTATTTACTTGT	43	328
994887	N/A	N/A	448332	448351	TCTAGTTTCCATAGCTTCCT	17	329
994895	N/A	N/A	450049	450068	TCTTTGTTTCTTTTTGCCTA	9	330
994903	N/A	N/A	451583	451602	TCCATTTTTGTTTAAAGGGT	25	331
994911	N/A	N/A	452493	452512	TGGTACAGATAATTGTGATG	29	332
994919	N/A	N/A	453190	453209	TGGATTTTATACACATTCAG	49	333
994927	N/A	N/A	456737	456756	CTTAGATTTTATGAGCTCAA	21	334

Table 6

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994312	105	124	2615	2634	GCTGCTGTTGCTCTGGCTGC	46	335
994320	418	437	106160	106179	CTCTTTCTCTCTTGTTCCTG	7	336
994328	562	581	178172	178191	ACCATAAGCTATCAGTTCCT	8	337
994336	916	935	435635	435654	GTCTGGATGGCTCTGATTTT	39	338
994344	974	993	435693	435712	TCCGCTCTTGGTTGGATTTC	63	339
994352	1637	1656	436356	436375	TGCTGAGGTGCTGCTGCTGC	31	340
994360	1927	1946	436646	436665	GTTCAGGACCTCCTTGGCCT	69	341
994368	2560	2579	437279	437298	CTCAGGGTTGAAGTTCTCGC	36	342
994376*	2758	2777	437477	437496	TGCACTCTGGATGAAATCTT	34	343
994384	3025	3044	457278	457297	CTTCAGGTTCTTGAGGGTAA	33	344
994392	3248	3267	457501	457520	GCTTGCTGGGTTCTATTTTG	93	345
994400	3546	3565	457799	457818	CCTGCTGTAACTCTAATGAC	40	346
994408	3987	4006	458240	458259	TGGTTAACTTTCCAAATCTG	16	347
994416	4283	4302	458536	458555	GTTTTCCTAACACTGCACAG	23	348
994424	4661	4680	458914	458933	ATGTAGTTACAGTGTTGAAA	5	349
994432	4777	4796	459030	459049	CAGGTAGTACTTGGTGGTCA	76	350
994440	5037	5056	459290	459309	ATTTTGCTACATTTATTTAT	53	351
994448	5496	5515	459749	459768	GTATTTGTTCAGTTTAGTTG	5	352
994456	5682	5701	459935	459954	GCTATTCTAAACCTATTCAA	75	353
994464	6029	6048	460282	460301	GGTTTAGTGGATCCAGTCAA	7	354
994472	6143	6162	460396	460415	AAGTGTTTAGAAAGAACCAA	41	355
994480	6702	6721	460955	460974	TGGCAGGTGGTCCCCTCCAC	68	356
994488	7064	7083	461317	461336	ATAGTATTATTTTTTTCTTT	68	357
994496	7095	7114	461348	461367	AGAGAGGTTCTTGTTTGTTG	6	358
994504	7447	7466	461700	461719	TGCTGCCACTTCCTGGTGGG	87	359
994512	8003	8022	462256	462275	GTCTGTTGAGCTGCTTGTGG	32	360
994520	8230	8249	462483	462502	CTCTGTATATTTATTACTTG	5	361
994528	8496	8515	462749	462768	ATTTTGTTTTCTTCAGCTTC	34	362
994536	8653	8672	462906	462925	CCTTCTCTGCTTTTTTTTTT	73	363
994544	8987	9006	463240	463259	GTTCAAGATTATATTCTTTG	21	364
994552	9235	9254	463488	463507	GTCCGGCTTGATTTTTGGAC	78	365
994560	9477	9496	463730	463749	TTGTTGTTATTGTATAGATA	21	366
994568	9935	9954	464188	464207	TTTAGAGTTGAGCAGTTCAG	20	367
994576	10167	10186	464420	464439	TGTCAGTCTGGTAGTGCCCT	18	368
994584	10362	10381	464615	464634	ATTTTTTAATATTTGTTTAA	75	369
994592	10604	10623	464857	464876	GTTATTTTATTAGTACGAGT	25	370
994600	205	224	9921	9940	GGTGCTTGTAGTAGTTTTTG	27	371
994608	N/A	N/A	22131	22150	TCCTCCTTTTATATCTGTTT	72	372
994616	N/A	N/A	39208	39227	GTTTGATTACTGTCATGACT	36	373

994624	N/A	N/A	51696	51715	GTGAAAAGAAAGATGTACTT	82	374
			51749	51768			
994632	N/A	N/A	85767	85786	CGTTGACTATCTTATTTTTT	26	375
994640	N/A	N/A	103358	103377	TCTCAATTATAATTTGTTTT	71	376
994648	N/A	N/A	118549	118568	GTTTCCTTAAAAGCAACTGT	24	377
994656	N/A	N/A	148250	148269	AGAGTCAATGATTAAATTCA	29	378
			149361	149380			
994664	N/A	N/A	148584	148603	CATGACTCTTTCTTAAGAAT	49	379
			149695	149714			
994672	N/A	N/A	149011	149030	AAATTTTCTAGAAACATTAA	60	380
			150122	150141			
994680	N/A	N/A	160737	160756	GTTACCATTCTCCTTTCCCC	50	381
994688	N/A	N/A	170872	170891	TGCTAGCTACAGAGCACTGA	122	382
			170939	170958			
994696	N/A	N/A	188547	188566	CGTTGGATATTTTATTCTTT	2	383
994704	N/A	N/A	213149	213168	ATGTTTGTATTCCATATTTG	20	384
994712	N/A	N/A	224696	224715	TCTTTTCATCTTCAGCTCTG	50	385
994720	N/A	N/A	264945	264964	GTTTGTGCTTTTGGTGTCAC	14	386
994728	N/A	N/A	275360	275379	GTTTGCTTTCTTCATCCTAC	45	387
994736	N/A	N/A	299651	299670	AATCGCAGGGAGGATTGAAA	47	388
			308026	308045			
994744	N/A	N/A	318885	318904	TGACCTTTATTTGGATCTTG	26	389
994752	N/A	N/A	329899	329918	TGGCATTTATAATATTTGTG	2	390
994760	N/A	N/A	347724	347743	ATTTTCTTAGAAGGATCTCT	10	391
994768	N/A	N/A	359649	359668	GTTTGAACTGAGCATGTTTT	17	392
994776	N/A	N/A	380393	380412	TGGTCATTAGATCATGCTAC	31	393
994784	N/A	N/A	396974	396993	TGTAGCTTTTAGTGACTTTG	11	394
994792	N/A	N/A	415670	415689	ATTTTGGCTTTCCATAGTGT	44	395
994800	N/A	N/A	434146	434165	GTTACTGCTGCTGTGTGGGC	64	396
994808	N/A	N/A	439027	439046	CTAGGATTAGCTAATTCCTA	78	397
994816	N/A	N/A	439709	439728	TCTCTACTAAAATGTTTTTT	43	398
994824	N/A	N/A	441169	441188	GGAGTATTTTAGCTGTGATG	6	399
994832	N/A	N/A	442536	442555	GCTTCCTTTGGTGCACGCAG	34	400
994840	N/A	N/A	444077	444096	GTTTGACATAGTTTCTCTGT	15	401
994848	N/A	N/A	444899	444918	TGGTGTGTACTTGTGGTCCC	49	402
994856	N/A	N/A	445653	445672	GTTTCAGTAAGTATGTCTTG	11	403
994864	N/A	N/A	446193	446212	GTTATAAGAGATCTGCCTAC	70	404
994872	N/A	N/A	446936	446955	ATCACACTTCAGTTATTTTC	31	405
994880	N/A	N/A	447652	447671	TCTTCTTATGCATTCTTTTT	29	406
994888	N/A	N/A	448391	448410	CCACCCACTGTCCTTTTCAG	58	407
994896	N/A	N/A	450077	450096	ATTCTTCTTTAATCACTTCA	55	408
994904	N/A	N/A	452108	452127	GTTTGCTTATTCTTGCCCAA	11	409
994912	N/A	N/A	452497	452516	TCCATGGTACAGATAATTGT	53	410
994920	N/A	N/A	453505	453524	GTTGGATTCTTTTTTTCTTT	5	411
994928	N/A	N/A	456851	456870	TCTATAGCTGGTCTCTGTTA	54	412

Table 7

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994313	111	130	2621	2640	CTTGCGGCTGCTGTTGCTCT	28	413
994321	419	438	106161	106180	ACTCTTTCTCTCTTGTTCCT	7	414
994329	590	609	178200	178219	GTACCATGTGCTTTCATCAC	11	415
994337	924	943	435643	435662	GTTTCACTGTCTGGATGGCT	21	416
994345	977	996	435696	435715	TGCTCCGCTCTTGGTTGGAT	57	417
994353	1693	1712	436412	436431	GTACTGGTTCTGCTGGGCTG	32	418
994361	1949	1968	436668	436687	GCCGGCTCTTCTCCATCTCA	87	419
994369	2720	2739	437439	437458	CCTTCTTTAGCTCCCCGTTG	48	420
994377*	2768	2787	437487	437506	TGCTTATCTCTGCACTCTGG	6	421
994385	3034	3053	457287	457306	AGAGCCGTTCTTCAGGTTCT	90	422
994393	3279	3298	457532	457551	GCCGACCACCTCCTCTTCCT	89	423
994401	3568	3587	457821	457840	TGCACCAGTCTCCTGCGACA	41	424
994409	3999	4018	458252	458271	TGTTCTTTTAAATGGTTAAC	17	425
994417	4330	4349	458583	458602	GTTTGCATCTACCTCTTGGG	14	426
994425	4673	4692	458926	458945	TGCAGAGCTGAAATGTAGTT	38	427
994433	4780	4799	459033	459052	CGTCAGGTAGTACTTGGTGG	55	428
994441	5069	5088	459322	459341	AATGGCCTAGAGTTTAGGCA	81	429
994449	5499	5518	459752	459771	CAGGTATTTGTTCAGTTTAG	3	430
994457	5905	5924	460158	460177	TCCTCTTACCATCAAAGGCT	45	431
994465	6033	6052	460286	460305	TGTTGGTTTAGTGGATCCAG	13	432
994473	6194	6213	460447	460466	TGGCACAGAAAGTATTGCAC	34	433
994481	6716	6735	460969	460988	GTGGTGACCGTGGGTGGCAG	84	434
994489	7075	7094	461328	461347	GTTTCTTATTAATAGTATTA	38	435
994497	7125	7144	461378	461397	GTCATTTTATATATTTAGAA	74	436
994505	7454	7473	461707	461726	GGAGGGATGCTGCCACTTCC	67	437
994513	8005	8024	462258	462277	CAGTCTGTTGAGCTGCTTGT	55	438
994521	8232	8251	462485	462504	TTCTCTGTATATTTATTACT	42	439
994529	8503	8522	462756	462775	CTTCAAAATTTTGTTTTCTT	38	440
994537	8693	8712	462946	462965	TGACAAATTTCTATATACAA	66	441
994545	9036	9055	463289	463308	TGAGTCCTGTTTGATTGGTA	8	442
994553	9244	9263	463497	463516	GTTTCCACTGTCCGGCTTGA	29	443
994561	9486	9505	463739	463758	TCTTAGAGATTGTTGTTATT	12	444
994569	9942	9961	464195	464214	ATTTGGGTTTAGAGTTGAGC	6	445
994577	10193	10212	464446	464465	TCCCTAGTTCTCCTCTGTAC	74	446
994585	10365	10384	464618	464637	TCCATTTTTTAATATTTGTT	27	447
994593	10606	10625	464859	464878	CTGTTATTTTATTAGTACGA	42	448
994601	206	225	9922	9941	TGGTGCTTGTAGTAGTTTTT	33	449
994609	N/A	N/A	22231	22250	TCTTCATTTTAATGTTGTTT	13	450

994617	N/A	N/A	39411	39430	TCTGCTCTAAAACTTTCTAC	55	451
994625	N/A	N/A	51702	51721	TTATTAGTGAAAAGAAAGAT	43	452
			51755	51774			
994633	N/A	N/A	86196	86215	ATTCAGATATAATTGTTTAC	69	453
994641	N/A	N/A	105012	105031	GTGTGAATAACTAATTCCTT	53	454
994649	N/A	N/A	120191	120210	TGTTTGATAAATGTTATTCT	11	455
994657	N/A	N/A	148273	148292	TATTATATTAAAAGTTAAAA	62	456
			149384	149403			
994665	N/A	N/A	148615	148634	AGAGGCTTCTGGAAATCCCC	49	457
			149726	149745			
994673	N/A	N/A	149065	149084	CCTGTCTTGATAAAATAAAA	96	458
			150161	150180			
994681	N/A	N/A	162490	162509	TGCATCTATTTTCTATTCTG	96	459
994689	N/A	N/A	176036	176055	GAAAATTCCTACTCATTTTT	99	460
			176352	176371			
994697	N/A	N/A	189098	189117	GTTTCTGCTAATCTGTGACA	31	461
994705	N/A	N/A	214840	214859	GTTTGCAGTTAACTTTTTTT	34	462
994713	N/A	N/A	226996	227015	TGGTTATTTACTCATTCTAC	19	463
994721	N/A	N/A	265218	265237	TCTTTTCATAAGCTTATTGG	71	464
994729	N/A	N/A	279331	279350	GTCTGCTTTCAATGAAGCAC	69	465
994737	N/A	N/A	299784	299803	ACTTTCCTGTCTTACAAGAG	19	466
			299827	299846			
994745	N/A	N/A	320275	320294	GTGAGAACTGCTATTTTCAG	7	467
994753	N/A	N/A	330357	330376	TCAGCTGTACAGCTCCTTAC	55	468
994761	N/A	N/A	347823	347842	TGGTCATTATCTAGTTTCTG	5	469
994769	N/A	N/A	365364	365383	GTGTGTCTAGTTTGTTTTTC	20	470
994777	N/A	N/A	380610	380629	GTTATATATTTCCTATTTTC	34	471
994785	N/A	N/A	398119	398138	TCTATATATTAATCATTTCC	68	472
994793	N/A	N/A	417738	417757	GGGTTATATCATGTTGGCCA	67	473
994801	N/A	N/A	437630	437649	CGGTGTGGTGTCCCATCCCT	71	474
994809	N/A	N/A	439072	439091	CTTTGATATTTTAGTGTCTT	12	475
994817	N/A	N/A	440059	440078	TCCTGATTTTCTTTTTTTTT	49	476
994825	N/A	N/A	441229	441248	TGCTCTCTGTCTGAGTCTCC	68	477
994833	N/A	N/A	442847	442866	GTGCCAGTTCCTGCATTTTC	43	478
994841	N/A	N/A	444080	444099	GTGGTTTGACATAGTTTCTC	6	479
994849	N/A	N/A	445236	445255	GTTTTTCTTACACATGGTAG	23	480
994857	N/A	N/A	445654	445673	GGTTTCAGTAAGTATGTCTT	8	481
994865	N/A	N/A	446197	446216	TGTGGTTATAAGAGATCTGC	28	482
994873	N/A	N/A	446951	446970	TCATGATTTTATTGAATCAC	26	483
994881	N/A	N/A	447992	448011	TCTTTATACCAGGGATCCCC	154	484
994889	N/A	N/A	448705	448724	TCATACTTTCTTCCGCTCTT	38	485
994897	N/A	N/A	450234	450253	GGGTTTCATTCACCATGTTG	47	486
994905	N/A	N/A	452110	452129	CGGTTTGCTTATTCTTGCCC	43	487
994913	N/A	N/A	452653	452672	ATTTTCTTTTTTCTGTGCCT	9	488
994921	N/A	N/A	453506	453525	TGTTGGATTCTTTTTTTCTT	12	489

994929	N/A	N/A	456930	456949	TGGGTTGTACCTCTACTTGC	69	490

Table 8

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994314	246	265	10657	10676	TGGTGACTTGATGCACGATG	10	491
994322	422	441	106164	106183	TCCACTCTTTCTCTCTTGTT	17	492
994330	687	706	277905	277924	TCTTTCTTCCTTTCACAGAG	35	493
994338	930	949	435649	435668	GTGACTGTTTCACTGTCTGG	79	494
994346	980	999	435699	435718	CGTTGCTCCGCTCTTGGTTG	47	495
994354	1870	1889	436589	436608	GGTGGCCTCCCGAGGGACAA	76	496
994362	2074	2093	436793	436812	ATCACGACTGCTGTAGTCTG	42	497
994370	2724	2743	437443	437462	TCCACCTTCTTTAGCTCCCC	71	498
994378*	2771	2790	437490	437509	CGTTGCTTATCTCTGCACTC	16	499
994386	3115	3134	457368	457387	GTGTCTGCTGCCCGCCAGGC	77	500
994394	3310	3329	457563	457582	TTCTGACTTCTCCAGTTTGC	75	501
994402	3618	3637	457871	457890	GTGCCCTTCCTCCCGCCCGC	77	502
994410	4028	4047	458281	458300	TTTATTGTAAAATATGTTGG	71	503
994418	4334	4353	458587	458606	GGCAGTTTGCATCTACCTCT	19	504
994426	4691	4710	458944	458963	CTTGCTCTTCAGCAATTCTG	52	505
994434	4824	4843	459077	459096	ATGCCTTGAACTGATTCTCA	13	506
994442	5218	5237	459471	459490	CTCACATATATAAATGTCTT	17	507
994450	5532	5551	459785	459804	AAAGTACTATTTTCAATGGG	23	508
994458	5915	5934	460168	460187	CAGCCCGTATTCCTCTTACC	19	509
994466	6034	6053	460287	460306	GTGTTGGTTTAGTGGATCCA	22	510
994474	6208	6227	460461	460480	TGGTCAGACTCTATTGGCAC	36	511
994482	6842	6861	461095	461114	TGTTTGCTACACAGAAGCGG	61	512
994490	7077	7096	461330	461349	TGGTTTCTTATTAATAGTAT	24	513
994498	7127	7146	461380	461399	CAGTCATTTTATATATTTAG	44	514
994506	7707	7726	461960	461979	GTGCAAAGAGTGGATTTTAT	6	515
994514	8063	8082	462316	462335	TGGCCCTGTTTTCACCTGGT	76	516
994522	8333	8352	462586	462605	GTTTGGAGTTTCCCTATGCC	13	517
994530	8509	8528	462762	462781	TGAGTGCTTCAAAATTTTGT	42	518
994538	8741	8760	462994	463013	GTAGTAATTCTTCCAGGCCA	25	519
994546	9047	9066	463300	463319	TGTCCCCATAATGAGTCCTG	32	520
994554	9249	9268	463502	463521	GTCCAGTTTCCACTGTCCGG	49	521
994562	9685	9704	463938	463957	GGACAGTATGTTATCTTGGT	8	522
994570	9953	9972	464206	464225	GGCTGACACTAATTTGGGTT	22	523
994578	10196	10215	464449	464468	CCTTCCCTAGTTCTCCTCTG	24	524
994586	10367	10386	464620	464639	CTTCCATTTTTTAATATTTG	38	525
994594	10608	10627	464861	464880	CACTGTTATTTTATTAGTAC	77	526
994602	N/A	N/A	5488	5507	ATAAAAGTTGAGTAGCTAGA	68	527

			6515	6534			
994610	N/A	N/A	28064	28083	TCCGCATTATTTTTCCCTGC	9	528
994618	N/A	N/A	40728	40747	TCCTACTTTTAAGTTTCCAG	10	529
994626	N/A	N/A	51710	51729	AAACTAATTTATTAGTGAAA	94	530
			51763	51782			
994634	N/A	N/A	86436	86455	TGTATAGTAGAATTTTTTTT	77	531
994642	N/A	N/A	106495	106514	GTGTGTTTAGTTGTTTGGGT	3	532
994650	N/A	N/A	122443	122462	GTTGAGACTTAATTGCTCAG	67	533
994658	N/A	N/A	149437	149456	GAATACTATGTATTTGCCAC	14	534
			148326	148345			
994666	N/A	N/A	149806	149825	TTTTGACAAGTCAGTCTTTT	87	535
			148695	148714			
994674	N/A	N/A	155493	155512	GTTTCCTTAAAATATGTTGG	9	536
994682	N/A	N/A	163871	163890	TCCATTGTATATGTATCTGT	26	537
994690	N/A	N/A	179789	179808	GTTATATTTAATCATGTTCC	13	538
994698	N/A	N/A	189111	189130	GTCATATTTCTTAGTTTCTG	4	539
994706	N/A	N/A	217284	217303	GTTATGTTTAAGGTATTTTC	21	540
994714	N/A	N/A	234290	234309	CGTCGGATAAATTTATCCAC	80	541
994722	N/A	N/A	265414	265433	GTTTTCTATAGTGATTGCAC	44	542
994730	N/A	N/A	281189	281208	TCTTTTTTTCTTTTAACCCT	6	543
994738	N/A	N/A	299793	299812	CAATCAGGAACTTTCCTGTC	65	544
			308168	308187			
994746	N/A	N/A	322234	322253	AGGAACACAAGAGGGAATAC	53	545
			323496	323515			
994754	N/A	N/A	331549	331568	TCTTTCCTAAAGCTTATTAG	52	546
994762	N/A	N/A	352034	352053	GTTTTAACTCAGCTCTCTCT	53	547
994770	N/A	N/A	366558	366577	CGGCTAGTATTTATATTTTT	48	548
994778	N/A	N/A	382060	382079	GTCTACATTTATAGATTTAG	11	549
994786	N/A	N/A	400669	400688	GTGTTACATAAATTAATTCC	14	550
994794	N/A	N/A	418949	418968	GTTACTGTTCTTATCTTGTG	47	551
994802	N/A	N/A	437850	437869	GGTGAGTTTCTGGATTGTCT	7	552
994810	N/A	N/A	439073	439092	GCTTTGATATTTTAGTGTCT	6	553
994818	N/A	N/A	440092	440111	TGAGCTGTATTATTATGCCA	68	554
994826	N/A	N/A	441272	441291	TCCAGATATGAGTTCTCTCT	28	555
994834	N/A	N/A	442868	442887	GTTCAGACTCAGATCTCTTC	27	556
994842	N/A	N/A	444247	444266	ATAGTCTTTAATTTTTTTCT	88	557
994850	N/A	N/A	445319	445338	GTGGAAGTGTTTCAGGGTTG	14	558
994858	N/A	N/A	445807	445826	TGTTGTTTAAATATGTCTCC	23	559
994866	N/A	N/A	446198	446217	GTGTGGTTATAAGAGATCTG	27	560
994874	N/A	N/A	447042	447061	CAGTGCTTTCTCCAGGGTGT	3	561
994882	N/A	N/A	447995	448014	TCCTCTTTATACCAGGGATC	47	562
994890	N/A	N/A	448758	448777	ATCTCCATAAATGGTATCCC	37	563
994898	N/A	N/A	450475	450494	GGAGAGAGAGAATATTTGAG	22	564
994906	N/A	N/A	452112	452131	TGCGGTTTGCTTATTCTTGC	14	565
994914	N/A	N/A	452981	453000	ACTTGAGTACATTCATATGG	57	566

994922	N/A	N/A	453610	453629	ATCTAGATTGAAGTTTGTAC	94	567
994930	N/A	N/A	456945	456964	TGAGGCTCTTCTCTTTGGGT	35	568

Table 9

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994315	295	314	10706	10725	ATTGCTGTACAAGGATGACA	16	569
994323	433	452	106175	106194	GCAGGCTGAAATCCACTCTT	20	570
994331	690	709	277908	277927	TGTTCTTTCTTCCTTTCACA	29	571
994339	932	951	435651	435670	CGGTGACTGTTTCACTGTCT	70	572
994347	1068	1087	435787	435806	CGGTGGTTGTCGCTGGGCAG	24	573
994355	1879	1898	436598	436617	AGCTTTCTTGGTGGCCTCCC	91	574
994363	2213	2232	436932	436951	GCTTCCCTAAATGCAGGCCA	64	575
994371	2727	2746	437446	437465	TCTTCCACCTTCTTTAGCTC	96	576
994379*	2812	2831	437531	437550	GTCTTCAATCCTCTCTACGG	3	577
994387	3127	3146	457380	457399	CTCGGCATACCTGTGTCTGC	58	578
994395	3313	3332	457566	457585	GTCTTCTGACTTCTCCAGTT	47	579
994403	3627	3646	457880	457899	GCTCCTGCTGTGCCCTTCCT	34	580
994411	4046	4065	458299	458318	ATACAATTAAAAGTTGCTTT	98	581
994419	4436	4455	458689	458708	ACCCGAGTTGTCCATAGTCA	12	582
994427	4701	4720	458954	458973	CTTTCAATATCTTGCTCTTC	25	583
994435	4856	4875	459109	459128	CTTTTCTCTCAGTTTCTCTG	23	584
994443	5219	5238	459472	459491	GCTCACATATATAAATGTCT	14	585
994451	5557	5576	459810	459829	TTTTTTTTTAATTTGTGAAA	95	586
994459	5979	5998	460232	460251	GTGTGTTTTTCTGAGTCCAC	3	587
994467	6040	6059	460293	460312	ATCTTAGTGTTGGTTTAGTG	14	588
994475	6231	6250	460484	460503	TGAGCTTTAACTATATAGCA	52	589
994483	6899	6918	461152	461171	TGGCTGATCCTTGTAAGCTG	64	590
994491	7080	7099	461333	461352	TGTTGGTTTCTTATTAATAG	12	591
994499	7151	7170	461404	461423	TCTTAAGTTAAACATTCTAA	49	592
994507	7839	7858	462092	462111	ATAGGTTTCCTTAGTAGTCA	17	593
994515	8068	8087	462321	462340	TCTGCTGGCCCTGTTTTCAC	23	594
994523	8356	8375	462609	462628	TCCGGAGTAGAGGTGTGCAA	68	595
994531	8510	8529	462763	462782	GTGAGTGCTTCAAAATTTTG	34	596
994539	8763	8782	463016	463035	GTATAGTTTAAGAGCCTTTT	8	597
994547	9121	9140	463374	463393	CATTGAAATCATGTTTTTAC	23	598
994555	9258	9277	463511	463530	CCCACAGCTGTCCAGTTTCC	62	599
994563	9700	9719	463953	463972	ACTTGGTATTCTGGAGGACA	6	600
994571	10096	10115	464349	464368	GGGTAATGATCTGATATTAA	5	601
994579	10239	10258	464492	464511	ATGCACTTAAAATTTTCTTT	10	602
994587	10368	10387	464621	464640	TCTTCCATTTTTTAATATTT	22	603
994595	10611	10630	464864	464883	TGGCACTGTTATTTTATTAG	41	604

994603	N/A	N/A	15303	15322	TGCTCATTAAATAATTGCAG	57	605
994611	N/A	N/A	28526	28545	GTGTCACTAGAAGATGCCCA	39	606
994619	N/A	N/A	41522	41541	GTGCTCACTAATAATAGTCT	21	607
994627	N/A	N/A	71054	71073	TCTCCTCTACTTAAGCTCAG	42	608
994635	N/A	N/A	87298	87317	GTTTCCTATCCTGATTCCCA	43	609
994643	N/A	N/A	106499	106518	GTTTGTGTGTTTAGTTGTTT	10	610
994651	N/A	N/A	127663	127682	GTGACCACTCTCCTCCTCCC	55	611
994659	N/A	N/A	148376	148395	AAGGTTTTCTCTTAAATATT	54	612
			149487	149506			
994667	N/A	N/A	148746	148765	TCCGAAGCTGCTATATGTCA	51	613
			149857	149876			
994675	N/A	N/A	155513	155532	GTGTGACACTATTATTCTTT	27	614
994683	N/A	N/A	169801	169820	CGACCTTTAAAATTTTTTCA	63	615
994691	N/A	N/A	180049	180068	ATTTGTTTACTTCTATATTG	65	616
994699	N/A	N/A	198910	198929	GCTTCTTTAAATCTTAGCTC	72	617
994707	N/A	N/A	218665	218684	GTTTGAGTCCAGTGACTTCT	44	618
994715	N/A	N/A	244999	245018	TCTTGAGTTTATCTTTTCTT	36	619
994723	N/A	N/A	269836	269855	CTCCAGTGCAGGGCTGGACT	86	620
			269865	269884			
			269894	269913			
994731	N/A	N/A	284231	284250	GTTTGGGTTTTTCTGTACAA	2	621
994739	N/A	N/A	305998	306017	TGGTAGGTATATAGATGTCC	3	622
994747	N/A	N/A	322370	322389	ATCCCAATAAAAACATTCAG	61	623
			323632	323651			
994755	N/A	N/A	331619	331638	TGTTCCATAGCTCATTTGCA	8	624
994763	N/A	N/A	353740	353759	TGCTGTGTACTTAATTGACA	41	625
994771	N/A	N/A	369407	369426	TCTTGTCTAGTTTTCTGCAG	54	626
994779	N/A	N/A	384151	384170	GTCATTTTTGAACATATCCT	11	627
994787	N/A	N/A	404260	404279	GTCTGTGTACCTCATTCTTT	13	628
994795	N/A	N/A	420137	420156	GTGTGGGTGGCTGTGTCCTG	70	629
994803	N/A	N/A	437851	437870	TGGTGAGTTTCTGGATTGTC	6	630
994811	N/A	N/A	439088	439107	CTTTTATTTTCTGATGCTTT	7	631
994819	N/A	N/A	440165	440184	GTAGTTCATTTTCTTTCTCC	6	632
994827	N/A	N/A	441275	441294	AAGTCCAGATATGAGTTCTC	25	633
994835	N/A	N/A	442870	442889	ATGTTCAGACTCAGATCTCT	26	634
994843	N/A	N/A	444248	444267	AATAGTCTTTAATTTTTTTC	88	635
994851	N/A	N/A	445325	445344	TCCTTGGTGGAAGTGTTTCA	57	636
994859	N/A	N/A	445808	445827	CTGTTGTTTAAATATGTCTC	15	637
994867	N/A	N/A	446255	446274	TCCTCCACTCTTTCCCTCCC	98	638
994875	N/A	N/A	447189	447208	GTTTGCCTTCTGTATGGAAA	12	639
994883	N/A	N/A	448112	448131	TGGAGCCTTGCTATGTTGGC	59	640
994891	N/A	N/A	448954	448973	TGGTTAAGACCTAGTTTCTT	42	641
994899	N/A	N/A	451089	451108	ATTTCTTGAGATGGATTCTC	24	642
994907	N/A	N/A	452123	452142	TCTACCAGAGTTGCGGTTTG	53	643
994915	N/A	N/A	453089	453108	CTTCATCTTCTTTGTTTCCT	36	644

994923	N/A	N/A	455414	455433	CATTCTTTTGAGTTGTGACC	31	645
994931	N/A	N/A	457057	457076	GTTTGATTTTATGCACACAC	63	646

Example 2: Effect of 5-10-5 MOE gapmer modified oligonucleotides on human ATXN1 RNA *in vitro*, single dose

Modified oligonucleotides complementary to human ATXN1 nucleic acid were designed and tested for their single dose effects on ATXN1 mRNA *in vitro*. The modified oligonucleotides were tested in a series of experiments that had similar culture conditions.

The modified oligonucleotides in the tables below are 5-10-5 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides and the 3' and 5' wings each consist of five 2'-MOE modified nucleosides. The motif for the gapmers is (from 5' to 3'): eeeeeddddddddddeeeee; wherein "d" represents a 2'-β-D-deoxyribosyl sugar, and 'e' represents a 2'-MOE modified ribosyl sugar. The internucleoside linkage motif for the gapmers is (from 5' to 3'): sooossssssssssooss; wherein 'o' represents a phosphodiester internucleoside linkage and 's' represents a phosphorothioate internucleoside linkage. Each cytosine residue is a 5-methyl cytosine.

"Start site" indicates the 5'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. "Stop site" indicates the 3'-most nucleoside to which the modified oligonucleotide is complementary in the human gene sequence. Each modified oligonucleotide listed in the Tables below is 100% complementary to SEQ ID NO: 1, SEQ ID NO: 2, or SEQ ID NO: 3 (GENBANK Accession No. NM_001128164.1). 'N/A' indicates that the modified oligonucleotide is not 100% complementary to that particular gene sequence.

Cultured A-431 cells were treated with modified oligonucleotide at a concentration of 4,000nM by free uptake at a density of 10,000 cells per well for a treatment period of 48 hours. At the end of their treatment period, total RNA was isolated from the cells and ATXN1 RNA levels were measured by quantitative real-time RTPCR. ATXN1 RNA levels were measured by Human ATXN1 primer probe set RTS37575 (forward sequence GTATAGGCTGAGGCTACCTGT, designated herein as SEQ ID NO: 14; reverse sequence GATCCAGGCTCTTCATGAGG, designated herein as SEQ ID NO: 15; probe sequence ACAGCAGCTCTGGATGAACATTCACT, designated herein as SEQ ID NO: 16). ATXN1 RNA levels were normalized to total RNA content, as measured by RIBOGREEN®. Results are presented in the tables below as percent ATXN1 RNA levels relative to untreated control cells (% Control). The Compound No. marked with an asterisk (*) indicates 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 10

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	4	138
1040079	468	487	N/A	N/A	AGACCAAAAACCATTTGTGT	9	647
1040111	2755	2774	437474	437493	ACTCTGGATGAAATCTTCTG	71	648

1040143	3244	3263	457497	457516	GCTGGGTTCTATTTTGGTGA	46	649
1040175	4029	4048	458282	458301	TTTTATTGTAAAATATGTTG	90	650
1040207	4510	4529	458763	458782	GATAGTAATATATGCTCATC	9	651
1040239	4767	4786	459020	459039	TTGGTGGTCATTTATTGTCA	8	652
1040271	5224	5243	459477	459496	ATCTTGCTCACATATATAAA	33	653
1040303	5589	5608	459842	459861	CTAGACAGCCAAAATGTGGG	29	654
1040335	6017	6036	460270	460289	CCAGTCAATTCAATACTCGA	14	655
1040367	6475	6494	460728	460747	CTCCACATTCACTATTCCGT	13	656
1040399	7152	7171	461405	461424	TTCTTAAGTTAAACATTCTA	75	657
1040431	7622	7641	461875	461894	GGAGTAATCCACAAGATGCA	48	658
1040463	8111	8130	462364	462383	TCCTTTCACATCACCACCGA	42	659
1040495	8375	8394	462628	462647	ATGTAAAAGAAATCTCAGCT	42	660
1040527	8696	8715	462949	462968	ACATGACAAATTTCTATATA	79	661
1040559	9109	9128	463362	463381	GTTTTTACTCCCCCCATTTA	106	662
1040591	9441	9460	463694	463713	TGCACTTAATTTTAATACAG	24	663
1040623	9885	9904	464138	464157	GGGCAGTATTCACAGAACTG	27	664
1040655	10254	10273	464507	464526	TCTTAACTATTATGTATGCA	18	665
1040687	10527	10546	464780	464799	TCAAATTTTGAATCAAACAT	88	666
1040719	N/A	N/A	17960	17979	TGAGTGCACATTTAATCTTT	11	667
1040751	N/A	N/A	31937	31956	TTGTCATATTTTTATAGCAT	76	668
1040783	N/A	N/A	51100	51119	TGTTCATTCCCTTAGTAACT	21	669
1040815	N/A	N/A	77282	77301	GGCAAGATCTTTTAAAGTCC	18	670
1040847	N/A	N/A	94809	94828	AGACTGTTTCTTTACCACAT	14	671
1040879	N/A	N/A	118132	118151	TCCACCAGTATTTATGGAGT	119	672
1040911	N/A	N/A	151437	151456	CTTTAGTATTTTTATCATTA	40	673
1040943	N/A	N/A	179378	179397	AACAGTACAATTTACTTGAC	56	674
1040975	N/A	N/A	195960	195979	CCTTTAAAAACCAACACAGT	84	675
1041007	N/A	N/A	216607	216626	TCTTGTCATTTTTAACATCC	28	676
1041039	N/A	N/A	237165	237184	ACTCAATTTTAAAGACTCGG	38	677
1041071	N/A	N/A	258705	258724	ATGTGTTGAATTTAACCAGC	22	678
1041103	N/A	N/A	276428	276447	CTCATTAATTAAATCATTCG	105	679
1041135	N/A	N/A	295010	295029	CACCTAAAAATACAGGAAGT	76	680
1041167	N/A	N/A	324809	324828	CCAAGAATTTAAAAAGGACA	42	681
1041199	N/A	N/A	345760	345779	TGTCTCAAACTATTCCCATT	26	682
1041231	N/A	N/A	371655	371674	TTAACAATCTTTTAGACCTG	24	683
1041263	N/A	N/A	393703	393722	GACATATTTCAAAAATGCAA	68	684
1041295	N/A	N/A	426181	426200	AACTTGTTTCAAAGTGAGAG	88	685
1041327	N/A	N/A	437896	437915	TCAGGGTTCCTCATCTTAAT	24	686
1041359	N/A	N/A	438301	438320	AGAGAGTATAAAAATTATCT	72	687
1041391	N/A	N/A	438910	438929	GCAGCCTCCTATATTGGTCC	40	688
1041423	N/A	N/A	439178	439197	CCAGTGACTCATCTTGGCTA	48	689
1041455	N/A	N/A	439863	439882	TGGTCCTTTCCTCACTTGGG	27	690
1041487	N/A	N/A	440220	440239	CATGTTTATTTTCCATGTGT	8	691
1041519	N/A	N/A	440788	440807	ACACACCTAGATCTTCCTCC	49	692
1041551	N/A	N/A	441387	441406	CAGCAGTGCCTAACCAGTTG	43	693

1041583	N/A	N/A	441652	441671	TGCCAGAGACCCAAATCCGC	64	694
1041615	N/A	N/A	442276	442295	TCATCCCCAAACTAAACACC	100	695
1041647	N/A	N/A	442821	442840	GCTAACCTACTTCCTACCCA	59	696
1041679	N/A	N/A	443177	443196	CATGACATCATTTAGCCTTA	12	697
1041711	N/A	N/A	443557	443576	GGCCCTAATAACACAGAGCC	113	698
1041743	N/A	N/A	444006	444025	GCGGCACAAATCCAGGGCTG	71	699
1041775	N/A	N/A	444407	444426	GTAGTATAAACTATGGACTT	26	700
1041807	N/A	N/A	445306	445325	AGGGTTGTTCAGTAAACCCA	134	701
1041839	N/A	N/A	445658	445677	GCTAGGTTTCAGTAAGTATG	9	702
1041871	N/A	N/A	445920	445939	ACACGCATATTTATGCTGTT	64	703
1041903	N/A	N/A	446128	446147	ACCTCCAACTCCCATTTTGG	54	704
1041935	N/A	N/A	446724	446743	GTAAATATATCCTGTTTCAA	59	705
1041967	N/A	N/A	446975	446994	TCACCTTGTCAGATGCTGAG	45	706
1041999	N/A	N/A	447909	447928	GGTGAGCAACCATTCCAGAC	74	707
1042031	N/A	N/A	448558	448577	CTCGGTCACCACATGCAAGC	102	708
1042063	N/A	N/A	448821	448840	GACCTAAAACACACCAGACC	78	709
1042095	N/A	N/A	449388	449407	ATAGCTTCAAAATATTGTTA	31	710
1042127	N/A	N/A	449700	449719	ATCTTTATTTTATAATTAGG	87	711
1042159	N/A	N/A	449981	450000	GATGCCACGACCAGATATCA	73	712
1042191	N/A	N/A	450575	450594	ACCAAACTCCAAATCTCCAA	38	713
1042223	N/A	N/A	451243	451262	TCAACCTTCTTGAACCCTCA	62	714
1042255	N/A	N/A	451690	451709	TCATTATTTCCGCATCTCAA	13	715
1042287	N/A	N/A	451970	451989	CCGGACACCTACCCATGGAG	82	716
1042319	N/A	N/A	452312	452331	CACTGTATTCTAAGTAGGAG	81	717
1042351	N/A	N/A	452637	452656	GCCTCCTGACCTCTACCCTT	56	718
1042383	N/A	N/A	453119	453138	AGTAGATTTCCACAGATTGT	26	719
1042415	N/A	N/A	453901	453920	AGCCTCTAGAACAAAATACA	97	720
1042447	N/A	N/A	455088	455107	AGCTTGAGAATTTTGATAGG	22	721
1042479	N/A	N/A	455365	455384	GAACCACAAGCCAACAGGCC	89	722
1042511	N/A	N/A	456665	456684	ACTGTGAGTTCCAAGAAGCA	49	723

Table 11

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040080*	824	843	435543	435562	TGGGTACAATCCGCCAACAG	32	724
1040112	2813	2832	437532	437551	TGTCTTCAATCCTCTCTACG	65	725
1040144	3334	3353	457587	457606	AGGAAGAGTCAAAGGTGGTT	41	726
1040176	4034	4053	458287	458306	GTTGCTTTTATTGTAAAATA	29	727
1040208	4512	4531	458765	458784	AAGATAGTAATATATGCTCA	11	728
1040240	4802	4821	459055	459074	CATCAAAGTGAAAAGTGCCT	48	729
1040272	5278	5297	459531	459550	CCATTCTGAAAATAACATTA	15	730

1040304	5614	5633	459867	459886	GGTGAACCCTAAATGTAAAT	40	731
1040336	6018	6037	460271	460290	TCCAGTCAATTCAATACTCG	26	732
1040368	6478	6497	460731	460750	ACACTCCACATTCACTATTC	55	733
1040400	7162	7181	461415	461434	ACTGAAATAATTCTTAAGTT	108	734
1040432	7653	7672	461906	461925	AGCATTATATTGCAATCTAT	31	735
1040464	8113	8132	462366	462385	TCTCCTTTCACATCACCACC	27	736
1040496	8385	8404	462638	462657	GAGGTCATCTATGTAAAAGA	15	737
1040528	8697	8716	462950	462969	GACATGACAAATTTCTATAT	12	738
1040560	9114	9133	463367	463386	ATCATGTTTTTACTCCCCCC	48	739
1040592	9454	9473	463707	463726	CCTATTGGCCAAATGCACTT	46	740
1040624	9970	9989	464223	464242	TCTTGAAACCTCCTTTCGGC	74	741
1040656	10255	10274	464508	464527	CTCTTAACTATTATGTATGC	25	742
1040688	10529	10548	464782	464801	GTTCAAATTTTGAATCAAAC	39	743
1040720	N/A	N/A	18197	18216	CCCAAATTTCAAAGGTCCTT	6	744
1040752	N/A	N/A	32181	32200	GTGGTCAAAGAATCTGTTTC	10	745
1040784	N/A	N/A	51766	51785	TAGAAACTAATTTATTAGTG	119	746
1040816	N/A	N/A	77793	77812	ACACAGATTATTTATAGTCA	13	747
1040848	N/A	N/A	96129	96148	CACTTTCTAGATTATTCTTA	84	748
1040880	N/A	N/A	118292	118311	ACTCTCTACCTTTAAGATTT	28	749
1040912	N/A	N/A	153619	153638	CATCTATTTATTTACCTTCT	30	750
1040944	N/A	N/A	179493	179512	GAACTTAAAATTCCCTAGGA	111	751
1040976	N/A	N/A	195968	195987	TCTTTTAACCTTTAAAAACC	53	752
1041008	N/A	N/A	216637	216656	ACCTGCTTTCAAAAGTCAAA	72	753
1041040	N/A	N/A	238066	238085	CAAGTAATACAAATCCACAG	65	754
1041072	N/A	N/A	259575	259594	CAGGACTTATTTTATATATG	32	755
1041104	N/A	N/A	276769	276788	CTTCCCAAATACATCATCGA	101	756
1041136	N/A	N/A	295238	295257	CATTTAAAAACTGTACATGG	20	757
1041168	N/A	N/A	324921	324940	ATCTAAATTTAAACTGCACA	31	758
1041200	N/A	N/A	347770	347789	TGGTCAATAATTTATATGGC	2	759
1041232	N/A	N/A	372753	372772	AACTATTATATTTATAGATT	108	760
1041264	N/A	N/A	395038	395057	AGCTGTAAAATATATCCCTG	8	761
1041296	N/A	N/A	427897	427916	AACCTTACTTAAATATCTCA	62	762
1041328	N/A	N/A	437897	437916	ATCAGGGTTCCTCATCTTAA	11	763
1041360	N/A	N/A	438322	438341	GTGCCCTTTCCTCTTGGGAT	58	764
1041392	N/A	N/A	438914	438933	CCCAGCAGCCTCCTATATTG	91	765
1041424	N/A	N/A	439182	439201	ACTTCCAGTGACTCATCTTG	34	766
1041456	N/A	N/A	439866	439885	ATTTGGTCCTTTCCTCACTT	28	767
1041488	N/A	N/A	440222	440241	CTCATGTTTATTTTCCATGT	31	768
1041520	N/A	N/A	440796	440815	AGGGAAAAACACACCTAGAT	39	769
1041552	N/A	N/A	441389	441408	GTCAGCAGTGCCTAACCAGT	41	770
1041584	N/A	N/A	441726	441745	ACAGAAAAACAAAACTCATT	105	771
1041616	N/A	N/A	442285	442304	CCTTAAAAATCATCCCCAAA	99	772
1041648	N/A	N/A	442823	442842	CAGCTAACCTACTTCCTACC	90	773
1041680	N/A	N/A	443212	443231	TCAGAAATACAGATTGATAT	44	774
1041712	N/A	N/A	443559	443578	ACGGCCCTAATAACACAGAG	94	775

1041744	N/A	N/A	444009	444028	ACTGCGGCACAAATCCAGGG	32	776
1041776	N/A	N/A	444408	444427	TGTAGTATAAACTATGGACT	23	777
1041808	N/A	N/A	445316	445335	GAAGTGTTTCAGGGTTGTTC	8	778
1041840	N/A	N/A	445659	445678	AGCTAGGTTTCAGTAAGTAT	7	779
1041872	N/A	N/A	445921	445940	TACACGCATATTTATGCTGT	98	780
1041904	N/A	N/A	446135	446154	AACTGTCACCTCCAACTCCC	57	781
1041936	N/A	N/A	446727	446746	CCAGTAAATATATCCTGTTT	26	782
1041968	N/A	N/A	446985	447004	CATAGCCACCTCACCTTGTC	72	783
1042000	N/A	N/A	447963	447982	GCAACAGACCAGTAGCAGTC	79	784
1042032	N/A	N/A	448600	448619	TACCTCCACCACCTTTGTCC	63	785
1042064	N/A	N/A	448823	448842	GTGACCTAAAACACACCAGA	37	786
1042096	N/A	N/A	449389	449408	GATAGCTTCAAAATATTGTT	20	787
1042128	N/A	N/A	449708	449727	GCAAATCTATCTTTATTTTA	79	788
1042160	N/A	N/A	449991	450010	CCTGCGAAAAGATGCCACGA	117	789
1042192	N/A	N/A	450674	450693	AAGTTCAGTTACAGAGGTGC	19	790
1042224	N/A	N/A	451247	451266	GTTCTCAACCTTCTTGAACC	110	791
1042256	N/A	N/A	451693	451712	CTTTCATTATTTCCGCATCT	14	792
1042288	N/A	N/A	451971	451990	GCCGGACACCTACCCATGGA	132	793
1042320	N/A	N/A	452314	452333	CCCACTGTATTCTAAGTAGG	82	794
1042352	N/A	N/A	452646	452665	TTTTTCTGTGCCTCCTGACC	59	795
1042384	N/A	N/A	453143	453162	AAGTACCAAAAAAACTTTAA	77	796
1042416	N/A	N/A	454243	454262	AGCCTCTAGAACAGGCTGGG	131	797
1042448	N/A	N/A	455090	455109	ACAGCTTGAGAATTTTGATA	21	798
1042480	N/A	N/A	455370	455389	ACAGTGAACCACAAGCCAAC	107	799
1042512	N/A	N/A	456692	456711	ACAGGACTAAACATGGATCA	39	800

Table 12

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	1	138
1040081*	856	875	435575	435594	ATCCAGGCTCTTCATGAGGA	5	801
1040113	2819	2838	437538	437557	TATGGCTGTCTTCAATCCTC	53	802
1040145	3369	3388	457622	457641	CAAATCTTAACCTCCTGAGG	48	803
1040177	4047	4066	458300	458319	TATACAATTAAAAGTTGCTT	110	804
1040209	4531	4550	458784	458803	CAGTATTTTTAAATGCTTAA	35	805
1040241	4815	4834	459068	459087	ACTGATTCTCAGACATCAAA	40	806
1040273	5279	5298	459532	459551	GCCATTCTGAAAATAACATT	9	807
1040305	5616	5635	459869	459888	CTGGTGAACCCTAAATGTAA	43	808
1040337	6019	6038	460272	460291	ATCCAGTCAATTCAATACTC	10	809
1040369	6480	6499	460733	460752	CCACACTCCACATTCACTAT	35	810
1040401	7190	7209	461443	461462	CCCCTCTGCCCCAGTGTGGC	96	811
1040433	7656	7675	461909	461928	TGCAGCATTATATTGCAATC	74	812

1040465	8114	8133	462367	462386	CTCTCCTTTCACATCACCAC	30	813
1040497	8417	8436	462670	462689	TCCTATCATCAGTAAGGTAA	92	814
1040529	8711	8730	462964	462983	AATCTGATCATTTAGACATG	42	815
1040561	9115	9134	463368	463387	AATCATGTTTTTACTCCCCC	76	816
1040593	9464	9483	463717	463736	ATAGATACTACCTATTGGCC	39	817
1040625	9971	9990	464224	464243	ATCTTGAAACCTCCTTTCGG	55	818
1040657	10257	10276	464510	464529	AGCTCTTAACTATTATGTAT	16	819
1040689	10559	10578	464812	464831	GTATACAGACAATTTATTTA	83	820
1040721	N/A	N/A	18359	18378	ACATGGTATTTTTATCAGTC	3	821
1040753	N/A	N/A	33291	33310	CCTAACAAAATTTCCCTTCA	73	822
1040785	N/A	N/A	53624	53643	GTGAATTTTCCTTAAATTTC	23	823
1040817	N/A	N/A	77899	77918	TGCAAATTCTAAAAATTACT	101	824
1040849	N/A	N/A	96635	96654	TTCTTGTTTCAAAGTGAGGA	121	825
1040881	N/A	N/A	118343	118362	GACCTCATCCATTATAATAT	52	826
1040913	N/A	N/A	153709	153728	CCAACCAACCAAAAACTCAC	101	827
1040945	N/A	N/A	179793	179812	CATAGTTATATTTAATCATG	64	828
1040977	N/A	N/A	196970	196989	ATGCCTCACCTTTAAATAGT	82	829
1041009	N/A	N/A	217125	217144	GACAAGTTTATTTATTTTTC	25	830
1041041	N/A	N/A	239500	239519	AACTGATTTCAAAGTCAGAC	131	831
1041073	N/A	N/A	260025	260044	ACTGAAACTTTTTAACATAC	37	832
1041105	N/A	N/A	278198	278217	CAGCAAATACAAACAGGACC	3	833
1041137	N/A	N/A	295336	295355	ACACAGTTACAAATCAATGC	1	834
1041169	N/A	N/A	324924	324943	TGGATCTAAATTTAAACTGC	6	835
1041201	N/A	N/A	348183	348202	ATGCTCAAACCTCATTCATT	23	836
1041233	N/A	N/A	373954	373973	TACTCCTTATTTTAAATATA	114	837
1041265	N/A	N/A	395428	395447	AAGGTTCTATTTTATATGCC	24	838
1041297	N/A	N/A	428019	428038	AGTGTTAGAGAATACTTTTC	33	839
1041329	N/A	N/A	437898	437917	AATCAGGGTTCCTCATCTTA	26	840
1041361	N/A	N/A	438362	438381	TGCCCCCCACTTTACGGTGT	98	841
1041393	N/A	N/A	438931	438950	CAGTCCAGAGCCCACTCCCC	96	842
1041425	N/A	N/A	439188	439207	AACCATACTTCCAGTGACTC	10	843
1041457	N/A	N/A	439897	439916	CCAGTCATTCACGAGTGGTT	60	844
1041489	N/A	N/A	440232	440251	TGACTCTTCACTCATGTTTA	67	845
1041521	N/A	N/A	440798	440817	GTAGGGAAAAACACACCTAG	87	846
1041553	N/A	N/A	441417	441436	CATTTCTGAATTTCTCTGTG	15	847
1041585	N/A	N/A	441728	441747	CCACAGAAAAACAAAACTCA	100	848
1041617	N/A	N/A	442286	442305	CCCTTAAAAATCATCCCCAA	103	849
1041649	N/A	N/A	442824	442843	GCAGCTAACCTACTTCCTAC	24	850
1041681	N/A	N/A	443215	443234	TACTCAGAAATACAGATTGA	62	851
1041713	N/A	N/A	443563	443582	ACAGACGGCCCTAATAACAC	106	852
1041745	N/A	N/A	444022	444041	TGTATTACCAACAACTGCGG	37	853
1041777	N/A	N/A	444419	444438	ACAGAGTGAACTGTAGTATA	3	854
1041809	N/A	N/A	445337	445356	AGCCTGACTCAGTCCTTGGT	122	855
1041841	N/A	N/A	445672	445691	GAATTCTCTCATAAGCTAGG	51	856
1041873	N/A	N/A	445928	445947	ATGCACATACACGCATATTT	57	857

1041905	N/A	N/A	446161	446180	CCATCCCCCTAAATCGACTC	84	858
1041937	N/A	N/A	446729	446748	ATCCAGTAAATATATCCTGT	15	859
1041969	N/A	N/A	447005	447024	GGCAGCTTTCTCAGCGGAGC	65	860
1042001	N/A	N/A	447978	447997	ATCCCCAACCCCCAGGCAAC	110	861
1042033	N/A	N/A	448602	448621	ACTACCTCCACCACCTTTGT	57	862
1042065	N/A	N/A	448825	448844	AAGTGACCTAAAACACACCA	88	863
1042097	N/A	N/A	449390	449409	TGATAGCTTCAAAATATTGT	30	864
1042129	N/A	N/A	449710	449729	TAGCAAATCTATCTTTATTT	70	865
1042161	N/A	N/A	450005	450024	AGGAGCTGTGTCACCCTGCG	71	866
1042193	N/A	N/A	450685	450704	CAGCCAAACCTAAGTTCAGT	32	867
1042225	N/A	N/A	451248	451267	AGTTCTCAACCTTCTTGAAC	78	868
1042257	N/A	N/A	451698	451717	AAAGCCTTTCATTATTTCCG	9	869
1042289	N/A	N/A	452004	452023	CCGGATAACTCCCTGTCTCC	80	870
1042321	N/A	N/A	452315	452334	ACCCACTGTATTCTAAGTAG	23	871
1042353	N/A	N/A	452658	452677	AACCCATTTTCTTTTTTCTG	119	872
1042385	N/A	N/A	453188	453207	GATTTTATACACATTCAGAC	58	873
1042417	N/A	N/A	454279	454298	CATCTTGTAAACTAAACAGG	58	874
1042449	N/A	N/A	455116	455135	GCTTACAATAATTAAGAAGA	60	875
1042481	N/A	N/A	455372	455391	AGACAGTGAACCACAAGCCA	95	876
1042513	N/A	N/A	456694	456713	GGACAGGACTAAACATGGAT	23	877

Table 13

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040082	896	915	435615	435634	AGTCTGATAAACGGAAAGTC	58	878
1040114	2839	2858	437558	437577	TATCACGGCCACGCCCGGGC	149	879
1040146	3372	3391	457625	457644	ATGCAAATCTTAACCTCCTG	12	880
1040178	4048	4067	458301	458320	CTATACAATTAAAAGTTGCT	111	881
1040210	4532	4551	458785	458804	ACAGTATTTTTAAATGCTTA	52	882
1040242	4816	4835	459069	459088	AACTGATTCTCAGACATCAA	39	883
1040274	5306	5325	459559	459578	GATTTGATTTTGAATAGAAA	64	884
1040306	5617	5636	459870	459889	CCTGGTGAACCCTAAATGTA	66	885
1040338	6025	6044	460278	460297	TAGTGGATCCAGTCAATTCA	22	886
1040370	6483	6502	460736	460755	TCTCCACACTCCACATTCAC	87	887
1040402	7241	7260	461494	461513	CACTTTAAAAGATCTGAGGT	51	888
1040434	7676	7695	461929	461948	GCTACTGTTCATCTTGAACA	76	889
1040466	8123	8142	462376	462395	AGTGTAATTCTCTCCTTTCA	17	890
1040498	8426	8445	462679	462698	AAGAAAAGATCCTATCATCA	76	891
1040530	8716	8735	462969	462988	ATACAAATCTGATCATTTAG	60	892
1040562	9116	9135	463369	463388	AAATCATGTTTTTACTCCCC	81	893
1040594	9466	9485	463719	463738	GTATAGATACTACCTATTGG	27	894

1040626	9991	10010	464244	464263	CCACAAATACTGACAGGACT	18	895
1040658	10258	10277	464511	464530	AAGCTCTTAACTATTATGTA	28	896
1040690	10561	10580	464814	464833	TGGTATACAGACAATTTATT	58	897
1040722	N/A	N/A	18895	18914	AACTTTAAAACCAAAGAGCC	89	898
1040754	N/A	N/A	33435	33454	TGTACAATAATATATTTCTT	63	899
1040786	N/A	N/A	53693	53712	GCAGAAATTCATTAAAAAGG	44	900
1040818	N/A	N/A	78103	78122	TACTGGTATATTTATTTGTT	25	901
1040850	N/A	N/A	96906	96925	CTTGAGTTTCATTATCTCCT	62	902
1040882	N/A	N/A	122955	122974	CATACATTCCCTTAAGCCAA	45	903
1040914	N/A	N/A	154008	154027	AGTATTATTTAAAACTACAT	107	904
1040946	N/A	N/A	180271	180290	CCATGGTTTCAAAGCTCTGT	68	905
1040978	N/A	N/A	198120	198139	AGCTATAAAATATAAACTTC	116	906
1041010	N/A	N/A	218069	218088	AGCTTTTGAATTTATTATGA	63	907
1041042	N/A	N/A	240054	240073	CAGAGACTATTTTAAAGACG	67	908
1041074	N/A	N/A	262925	262944	CTCTTATTTTAAACTGGTGC	17	909
1041106	N/A	N/A	279276	279295	TTACTGATTATTTAACCCTG	1	910
1041138	N/A	N/A	296194	296213	AGTTCATTTTAAACTGTATT	1	911
1041170	N/A	N/A	326365	326384	TGTATTATTTTCTAACAGAA	17	912
1041202	N/A	N/A	349100	349119	AAGTATACAATTTAAGGATC	18	913
1041234	N/A	N/A	374001	374020	ATTAGATTTCCTTACTGCAA	16	914
1041266	N/A	N/A	395704	395723	CCTCTCAAAACCACTTTTAT	123	915
1041298	N/A	N/A	428253	428272	CCCTCAATTCAAAGACAAAT	128	916
1041330	N/A	N/A	437904	437923	TTTCCTAATCAGGGTTCCTC	24	917
1041362	N/A	N/A	438363	438382	GTGCCCCCCACTTTACGGTG	35	918
1041394	N/A	N/A	438955	438974	CCTGACTTTCATATGCAAAC	23	919
1041426	N/A	N/A	439190	439209	TTAACCATACTTCCAGTGAC	49	920
1041458	N/A	N/A	439905	439924	CCCCATATCCAGTCATTCAC	91	921
1041490	N/A	N/A	440236	440255	GCAATGACTCTTCACTCATG	49	922
1041522	N/A	N/A	440800	440819	GAGTAGGGAAAAACACACCT	49	923
1041554	N/A	N/A	441434	441453	AAGCTCAACAATTTGCACAT	37	924
1041586	N/A	N/A	441742	441761	ACGAACACAAAAACCCACAG	65	925
1041618	N/A	N/A	442287	442306	CCCCTTAAAAATCATCCCCA	84	926
1041650	N/A	N/A	442825	442844	AGCAGCTAACCTACTTCCTA	34	927
1041682	N/A	N/A	443218	443237	TCATACTCAGAAATACAGAT	19	928
1041714	N/A	N/A	443616	443635	TTAAGCAGCCACCGAGTCAG	94	929
1041746	N/A	N/A	444023	444042	GTGTATTACCAACAACTGCG	8	930
1041778	N/A	N/A	444443	444462	TTCATCAAAAACAGCATGTA	85	931
1041810	N/A	N/A	445344	445363	CACGCAAAGCCTGACTCAGT	50	932
1041842	N/A	N/A	445673	445692	TGAATTCTCTCATAAGCTAG	96	933
1041874	N/A	N/A	445931	445950	ACTATGCACATACACGCATA	108	934
1041906	N/A	N/A	446163	446182	ATCCATCCCCCTAAATCGAC	54	935
1041938	N/A	N/A	446730	446749	CATCCAGTAAATATATCCTG	17	936
1041970	N/A	N/A	447020	447039	CTTTACCGCCTAACAGGCAG	123	937
1042002	N/A	N/A	447979	447998	GATCCCCAACCCCCAGGCAA	94	938
1042034	N/A	N/A	448606	448625	TTTTACTACCTCCACCACCT	61	939

1042066	N/A	N/A	448836	448855	ACTCAAACTTAAAGTGACCT	66	940
1042098	N/A	N/A	449409	449428	TGGGTATTCTCTATGATGCT	26	941
1042130	N/A	N/A	449713	449732	TCATAGCAAATCTATCTTTA	74	942
1042162	N/A	N/A	450017	450036	GCTTCCTACCAAAGGAGCTG	128	943
1042194	N/A	N/A	450686	450705	GCAGCCAAACCTAAGTTCAG	78	944
1042226	N/A	N/A	451252	451271	AAGAAGTTCTCAACCTTCTT	91	945
1042258	N/A	N/A	451699	451718	GAAAGCCTTTCATTATTTCC	29	946
1042290	N/A	N/A	452046	452065	TAGTTCCAAACATGTCAGCC	29	947
1042322	N/A	N/A	452353	452372	GACAAATATACTTACAAGTG	17	948
1042354	N/A	N/A	452664	452683	CCCCCAAACCCATTTTCTTT	121	949
1042386	N/A	N/A	453191	453210	TTGGATTTTATACACATTCA	45	950
1042418	N/A	N/A	454294	454313	GCTATAAATCAAAGACATCT	61	951
1042450	N/A	N/A	455117	455136	TGCTTACAATAATTAAGAAG	75	952
1042482	N/A	N/A	455402	455421	TTGTGACCCCAAAGCACTGT	100	953
1042514	N/A	N/A	456708	456727	GCTATTATCATACAGGACAG	20	954

Table 14

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040083	902	921	435621	435640	GATTTTAGTCTGATAAACGG	32	955
1040115	2852	2871	437571	437590	CGACGGCGAACTGTATCACG	120	956
1040147	3386	3405	457639	457658	TAGACCGGCCTTCAATGCAA	41	957
1040179	4050	4069	458303	458322	ATCTATACAATTAAAAGTTG	116	958
1040211	4534	4553	458787	458806	GAACAGTATTTTTAAATGCT	13	959
1040243	4817	4836	459070	459089	GAACTGATTCTCAGACATCA	15	960
1040275	5323	5342	459576	459595	ACCAAACATTAAATCTCGAT	36	961
1040307	5636	5655	459889	459908	GTTTATAAAAATCATTAGTC	76	962
1040339	6064	6083	460317	460336	GCTCCAAACCATGTGTGTTT	23	963
1040371	6493	6512	460746	460765	GCCTCCTTCCTCTCCACACT	54	964
1040403	7244	7263	461497	461516	TTCCACTTTAAAAGATCTGA	34	965
1040435	7696	7715	461949	461968	GGATTTTATGATTACTAGGA	9	966
1040467	8151	8170	462404	462423	GGCCTCCACGCCACTTAAAA	144	967
1040499	8432	8451	462685	462704	TGCTACAAGAAAAGATCCTA	63	968
1040531	8722	8741	462975	462994	ATAACCATACAAATCTGATC	61	969
1040563	9124	9143	463377	463396	TTACATTGAAATCATGTTTT	48	970
1040595	9467	9486	463720	463739	TGTATAGATACTACCTATTG	53	971
1040627	9996	10015	464249	464268	GGTCACCACAAATACTGACA	29	972
1040659	10269	10288	464522	464541	TGTCACAATAAAAGCTCTTA	47	973
1040691	10563	10582	464816	464835	ACTGGTATACAGACAATTTA	80	974
1040723	N/A	N/A	19256	19275	CCCAGCAAAGCCATCCAGTG	80	975
1040755	N/A	N/A	33606	33625	TTGATTACAATTTAAATTCA	90	976

1040787	N/A	N/A	54456	54475	AAGGGAATATTTTACTTTAT	13	977
1040819	N/A	N/A	78391	78410	CTATTATTATTTTACTGGCA	7	978
1040851	N/A	N/A	97882	97901	TTTTATAGCCACTAACCAAC	96	979
1040883	N/A	N/A	125349	125368	AACATATTTCATTATAATTC	100	980
1040915	N/A	N/A	154957	154976	ACCCAGCATTTTTAACATTA	63	981
1040947	N/A	N/A	180483	180502	CTTTCATTTATTTAGTGAAA	116	982
1040979	N/A	N/A	200076	200095	TTCCTTACTTTTTAGGATAC	119	983
1041011	N/A	N/A	218138	218157	GATTTATTTTAAAGTACTCT	83	984
1041043	N/A	N/A	241942	241961	GATTCCAAAACCAGACTTGT	143	985
1041075	N/A	N/A	263175	263194	CCATATATAGATTACAAAGC	39	986
1041107	N/A	N/A	281181	281200	TCTTTTAACCCTAAGACTGT	67	987
1041139	N/A	N/A	296440	296459	TGACAGTATTTTTAAAGACT	2	988
1041171	N/A	N/A	326617	326636	ACTGGCAAACCCAAAAGCTA	103	989
1041203	N/A	N/A	349644	349663	ACTGTTAAAACCCATCCAAC	63	990
1041235	N/A	N/A	374559	374578	ATGCAGTTCTAAAAGAAAGC	66	991
1041267	N/A	N/A	397171	397190	AGGCCCAAACCTCTAATCAA	123	992
1041299	N/A	N/A	429792	429811	AAGATTCAAATATATCTTAA	130	993
1041331	N/A	N/A	437924	437943	GGACCTGAAGTCCAGCAGCG	60	994
1041363	N/A	N/A	438401	438420	ACTCCCTCCACCTCCTGACC	101	995
1041395	N/A	N/A	438956	438975	GCCTGACTTTCATATGCAAA	45	996
1041427	N/A	N/A	439210	439229	GCCTGTGGAAATTAAGAGCG	101	997
1041459	N/A	N/A	439912	439931	TGCAAGCCCCCATATCCAGT	45	998
1041491	N/A	N/A	440261	440280	TTAAGGATTCTAAGTACCAT	20	999
1041523	N/A	N/A	440821	440840	TCATTAATTTTGCAAAGTTT	19	1000
1041555	N/A	N/A	441445	441464	TTTTGCTTATTAAGCTCAAC	49	1001
1041587	N/A	N/A	441743	441762	AACGAACACAAAAACCCACA	105	1002
1041619	N/A	N/A	442289	442308	AGCCCCTTAAAAATCATCCC	116	1003
1041651	N/A	N/A	442826	442845	AAGCAGCTAACCTACTTCCT	53	1004
1041683	N/A	N/A	443220	443239	GTTCATACTCAGAAATACAG	33	1005
1041715	N/A	N/A	443625	443644	CACTGAATATTAAGCAGCCA	76	1006
1041747	N/A	N/A	444024	444043	TGTGTATTACCAACAACTGC	69	1007
1041779	N/A	N/A	444458	444477	ACATGACATCATAAATTCAT	38	1008
1041811	N/A	N/A	445353	445372	AATCATGTTCACGCAAAGCC	41	1009
1041843	N/A	N/A	445675	445694	AATGAATTCTCTCATAAGCT	69	1010
1041875	N/A	N/A	445943	445962	CTATATCTAAACACTATGCA	79	1011
1041907	N/A	N/A	446164	446183	CATCCATCCCCCTAAATCGA	100	1012
1041939	N/A	N/A	446731	446750	TCATCCAGTAAATATATCCT	21	1013
1041971	N/A	N/A	447021	447040	GCTTTACCGCCTAACAGGCA	92	1014
1042003	N/A	N/A	447994	448013	CCTCTTTATACCAGGGATCC	83	1015
1042035	N/A	N/A	448607	448626	TTTTTACTACCTCCACCACC	93	1016
1042067	N/A	N/A	448839	448858	GCAACTCAAACTTAAAGTGA	46	1017
1042099	N/A	N/A	449410	449429	ATGGGTATTCTCTATGATGC	22	1018
1042131	N/A	N/A	449715	449734	ATTCATAGCAAATCTATCTT	102	1019
1042163	N/A	N/A	450018	450037	TGCTTCCTACCAAAGGAGCT	129	1020
1042195	N/A	N/A	450687	450706	AGCAGCCAAACCTAAGTTCA	61	1021

1042227	N/A	N/A	451307	451326	ACCCTCTATTAAAAATACTA	113	1022
1042259	N/A	N/A	451702	451721	TTTGAAAGCCTTTCATTATT	85	1023
1042291	N/A	N/A	452049	452068	CCTTAGTTCCAAACATGTCA	42	1024
1042323	N/A	N/A	452358	452377	ACATAGACAAATATACTTAC	31	1025
1042355	N/A	N/A	452665	452684	GCCCCCAAACCCATTTTCTT	113	1026
1042387	N/A	N/A	453354	453373	ATGCACCACCACCACCACGC	79	1027
1042419	N/A	N/A	454295	454314	TGCTATAAATCAAAGACATC	93	1028
1042451	N/A	N/A	455129	455148	TTACAAAGACTATGCTTACA	68	1029
1042483	N/A	N/A	455404	455423	AGTTGTGACCCCAAAGCACT	94	1030
1042515	N/A	N/A	456709	456728	TGCTATTATCATACAGGACA	21	1031

Table 15

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040084	909	928	435628	435647	TGGCTCTGATTTTAGTCTGA	34	1032
1040116	2895	2914	457148	457167	TACTCTACCAAAACTTCAAC	75	1033
1040148	3387	3406	457640	457659	TTAGACCGGCCTTCAATGCA	39	1034
1040180	4134	4153	458387	458406	GCAGAAATGAAATCCCGCAT	31	1035
1040212	4586	4605	458839	458858	TGAGATACAGTACTTGTTGA	12	1036
1040244	4866	4885	459119	459138	TTCTCCATCCCTTTTCTCTC	25	1037
1040276	5325	5344	459578	459597	GTACCAAACATTAAATCTCG	43	1038
1040308	5638	5657	459891	459910	CGGTTTATAAAAATCATTAG	80	1039
1040340	6065	6084	460318	460337	TGCTCCAAACCATGTGTGTT	42	1040
1040372	6500	6519	460753	460772	TGAATCTGCCTCCTTCCTCT	29	1041
1040404	7245	7264	461498	461517	TTTCCACTTTAAAAGATCTG	51	1042
1040436	7699	7718	461952	461971	AGTGGATTTTATGATTACTA	9	1043
1040468	8176	8195	462429	462448	GGTTAAAAACAAATGTGGAA	132	1044
1040500	8481	8500	462734	462753	GCTTCTCAAATCAGGTGTAC	11	1045
1040532	8726	8745	462979	462998	GGCCATAACCATACAAATCT	74	1046
1040564	9177	9196	463430	463449	GGCCTCTTTATATTAAATAA	135	1047
1040596	9510	9529	463763	463782	TCAGATAAGAAAAGTTATGG	54	1048
1040628	9997	10016	464250	464269	AGGTCACCACAAATACTGAC	36	1049
1040660	10275	10294	464528	464547	TTCTCCTGTCACAATAAAAG	93	1050
1040692	10565	10584	464818	464837	GTACTGGTATACAGACAATT	95	1051
1040724	N/A	N/A	20058	20077	GTCCTCAAAACCTATGGAGC	127	1052
1040756	N/A	N/A	34396	34415	TGGCTTAACCAGGGAGATGT	13	1053
1040788	N/A	N/A	56211	56230	ACTGATAATTTTTAGACATA	41	1054
1040820	N/A	N/A	79273	79292	ACCTCAATCATTTACTCTCT	22	1055
1040852	N/A	N/A	99200	99219	ACTCCTAAAATTTATTGAGG	124	1056
1040884	N/A	N/A	127408	127427	CCCTGAATAGTCTATGCCAT	37	1057
1040916	N/A	N/A	155491	155510	TTCCTTAAAATATGTTGGCA	43	1058

1040948	N/A	N/A	181346	181365	GGAAACAACCAAAAACTGCT	32	1059
1040980	N/A	N/A	202475	202494	TGACACAATATTTACTGTGT	99	1060
1041012	N/A	N/A	218314	218333	TCTCAGTTTCAAAATAGGAC	32	1061
1041044	N/A	N/A	241960	241979	CCTCAAAAAGAATCTGCAGA	102	1062
1041076	N/A	N/A	263468	263487	TCGGTTACTATTTACCTTTC	60	1063
1041108	N/A	N/A	281316	281335	GGACCCTAAATTTAAACAGC	2	1064
1041140	N/A	N/A	296918	296937	TGGAAATTTCAAAAAGCTAA	32	1065
1041172	N/A	N/A	327619	327638	AACAACAAATAATTACCTAT	114	1066
1041204	N/A	N/A	350026	350045	AAGGAAAATCAAACATTGCT	7	1067
1041236	N/A	N/A	375439	375458	AGGTCTAGTATTTATCTTCT	1	1068
1041268	N/A	N/A	398360	398379	GAAACATTATTTTACTTTTC	65	1069
1041300	N/A	N/A	430468	430487	TCCTAAAAATACATCTTAAA	102	1070
1041332	N/A	N/A	437957	437976	CTGGTAAGAAAAAGTGCCGA	120	1071
1041364	N/A	N/A	438416	438435	GCCACATTTCCCCTCACTCC	23	1072
1041396	N/A	N/A	438957	438976	AGCCTGACTTTCATATGCAA	56	1073
1041428	N/A	N/A	439250	439269	GTAATCGATCTAAGAACCTG	21	1074
1041460	N/A	N/A	439916	439935	TTTGTGCAAGCCCCCATATC	103	1075
1041492	N/A	N/A	440277	440296	TGTTCACAAAAATGTGTTAA	71	1076
1041524	N/A	N/A	440828	440847	CATTTAATCATTAATTTTGC	63	1077
1041556	N/A	N/A	441446	441465	ATTTTGCTTATTAAGCTCAA	38	1078
1041588	N/A	N/A	441811	441830	CCAATGATCCCATCACTGCA	103	1079
1041620	N/A	N/A	442290	442309	CAGCCCCTTAAAAATCATCC	105	1080
1041652	N/A	N/A	442846	442865	TGCCAGTTCCTGCATTTTCC	8	1081
1041684	N/A	N/A	443222	443241	CAGTTCATACTCAGAAATAC	50	1082
1041716	N/A	N/A	443626	443645	GCACTGAATATTAAGCAGCC	93	1083
1041748	N/A	N/A	444025	444044	GTGTGTATTACCAACAACTG	16	1084
1041780	N/A	N/A	444459	444478	TACATGACATCATAAATTCA	56	1085
1041812	N/A	N/A	445359	445378	ACACTGAATCATGTTCACGC	7	1086
1041844	N/A	N/A	445679	445698	GAGCAATGAATTCTCTCATA	27	1087
1041876	N/A	N/A	445945	445964	TACTATATCTAAACACTATG	115	1088
1041908	N/A	N/A	446169	446188	TCCTCCATCCATCCCCCTAA	75	1089
1041940	N/A	N/A	446740	446759	CCCATTTTTTCATCCAGTAA	12	1090
1041972	N/A	N/A	447022	447041	GGCTTTACCGCCTAACAGGC	107	1091
1042004	N/A	N/A	447996	448015	CTCCTCTTTATACCAGGGAT	85	1092
1042036	N/A	N/A	448608	448627	TTTTTTACTACCTCCACCAC	105	1093
1042068	N/A	N/A	448842	448861	TGGGCAACTCAAACTTAAAG	57	1094
1042100	N/A	N/A	449424	449443	AATTTAAAACCCATATGGGT	115	1095
1042132	N/A	N/A	449743	449762	CACACATCTCAAATAGGTAC	54	1096
1042164	N/A	N/A	450034	450053	GCCTAAATTCTGCCTTTGCT	35	1097
1042196	N/A	N/A	450690	450709	GTGAGCAGCCAAACCTAAGT	45	1098
1042228	N/A	N/A	451308	451327	AACCCTCTATTAAAAATACT	111	1099
1042260	N/A	N/A	451730	451749	CTAAAGACTTCATAATGTTA	58	1100
1042292	N/A	N/A	452051	452070	AGCCTTAGTTCCAAACATGT	107	1101
1042324	N/A	N/A	452368	452387	GTGCATATATACATAGACAA	8	1102
1042356	N/A	N/A	452666	452685	GGCCCCCAAACCCATTTTCT	114	1103

1042388	N/A	N/A	453520	453539	AATATTTAAAATATTGTTGG	120	1104
1042420	N/A	N/A	454296	454315	CTGCTATAAATCAAAGACAT	74	1105
1042452	N/A	N/A	455135	455154	TAGACTTTACAAAGACTATG	46	1106
1042484	N/A	N/A	455425	455444	CTGGTGAGCCCCATTCTTTT	39	1107
1042516	N/A	N/A	456710	456729	CTGCTATTATCATACAGGAC	18	1108

Table 16

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040085	964	983	435683	435702	GTTGGATTTCATTTTTCGCC	21	1109
1040117	2896	2915	457149	457168	ATACTCTACCAAAACTTCAA	90	1110
1040149	3411	3430	457664	457683	CCACGCTGCCTCTACTTGCC	49	1111
1040181	4135	4154	458388	458407	AGCAGAAATGAAATCCCGCA	33	1112
1040213	4588	4607	458841	458860	AGTGAGATACAGTACTTGTT	11	1113
1040245	4889	4908	459142	459161	ACTGGACAAAAATGAGTATT	39	1114
1040277	5326	5345	459579	459598	TGTACCAAACATTAAATCTC	53	1115
1040309	5639	5658	459892	459911	ACGGTTTATAAAAATCATTA	71	1116
1040341	6066	6085	460319	460338	TTGCTCCAAACCATGTGTGT	37	1117
1040373	6641	6660	460894	460913	CCACACTTCCCGTCCAGGCT	19	1118
1040405	7293	7312	461546	461565	CCAACATAGAAAATTATCCT	27	1119
1040437	7702	7721	461955	461974	AAGAGTGGATTTTATGATTA	26	1120
1040469	8177	8196	462430	462449	GGGTTAAAAACAAATGTGGA	67	1121
1040501	8482	8501	462735	462754	AGCTTCTCAAATCAGGTGTA	14	1122
1040533	8732	8751	462985	463004	CTTCCAGGCCATAACCATAC	23	1123
1040565	9179	9198	463432	463451	CTGGCCTCTTTATATTAAAT	83	1124
1040597	9518	9537	463771	463790	GAGTCCTTTCAGATAAGAAA	18	1125
1040629	10046	10065	464299	464318	CTCTGGAGCCAGGACTCCAC	111	1126
1040661	10289	10308	464542	464561	CATATGGAAAAAAGTTCTCC	69	1127
1040693	10566	10585	464819	464838	TGTACTGGTATACAGACAAT	79	1128
1040725	N/A	N/A	21690	21709	CCAATAAAAGCCACAACTTG	101	1129
1040757	N/A	N/A	34751	34770	AAGGTGTATATTTATATGTT	9	1130
1040789	N/A	N/A	56964	56983	GCTCAAATTCAAAAGATGAA	44	1131
1040821	N/A	N/A	79281	79300	TCAGTAAAACCTCAATCATT	51	1132
1040853	N/A	N/A	100126	100145	TGGAATATTCTTTATTTTGG	68	1133
1040885	N/A	N/A	127831	127850	TTACTCTTTCAAATGCAAAA	124	1134
1040917	N/A	N/A	157778	157797	AGGTTCTATATTTAGAACAC	143	1135
1040949	N/A	N/A	181515	181534	CTCACAATTCAAAAGTTGTG	93	1136
1040981	N/A	N/A	203086	203105	TTAGTCAAACATATCAACCT	52	1137
1041013	N/A	N/A	218395	218414	GGCTGCAAACTATTCAAGTA	99	1138
1041045	N/A	N/A	242013	242032	TCATTATTAGATTACCAAGA	36	1139
1041077	N/A	N/A	263601	263620	CAGTAATTTCAAAAGGGCCA	139	1140

1041109	N/A	N/A	281523	281542	TGGATGCTATTTTATGTAGA	3	1141
1041141	N/A	N/A	304301	304320	GACCACAAAACCCAACTTAC	41	1142
1041173	N/A	N/A	329293	329312	TCAACAAATCAAATACTGAT	94	1143
1041205	N/A	N/A	350846	350865	TGCTGCATATTTTATATTTA	21	1144
1041237	N/A	N/A	375452	375471	AGTGTATTAGATTAGGTCTA	3	1145
1041269	N/A	N/A	399227	399246	CTCCTTAAACCCCATTTTAT	79	1146
1041301	N/A	N/A	430469	430488	CTCCTAAAAATACATCTTAA	129	1147
1041333	N/A	N/A	437958	437977	CCTGGTAAGAAAAAGTGCCG	126	1148
1041365	N/A	N/A	438420	438439	GTTTGCCACATTTCCCCTCA	20	1149
1041397	N/A	N/A	438974	438993	CAGAGCTAATTCCTAGGAGC	35	1150
1041429	N/A	N/A	439254	439273	GCATGTAATCGATCTAAGAA	16	1151
1041461	N/A	N/A	439954	439973	TTCAGGGCTAAAAGCTCTCG	113	1152
1041493	N/A	N/A	440278	440297	CTGTTCACAAAAATGTGTTA	54	1153
1041525	N/A	N/A	440829	440848	TCATTTAATCATTAATTTTG	109	1154
1041557	N/A	N/A	441447	441466	GATTTTGCTTATTAAGCTCA	23	1155
1041589	N/A	N/A	441816	441835	GTGAGCCAATGATCCCATCA	68	1156
1041621	N/A	N/A	442291	442310	TCAGCCCCTTAAAAATCATC	127	1157
1041653	N/A	N/A	442874	442893	GGATATGTTCAGACTCAGAT	7	1158
1041685	N/A	N/A	443223	443242	CCAGTTCATACTCAGAAATA	61	1159
1041717	N/A	N/A	443628	443647	TGGCACTGAATATTAAGCAG	52	1160
1041749	N/A	N/A	444026	444045	AGTGTGTATTACCAACAACT	13	1161
1041781	N/A	N/A	444482	444501	CTGTATAATAATGTAATGCT	6	1162
1041813	N/A	N/A	445369	445388	TCTATTTAAAACACTGAATC	88	1163
1041845	N/A	N/A	445681	445700	GGGAGCAATGAATTCTCTCA	111	1164
1041877	N/A	N/A	445946	445965	CTACTATATCTAAACACTAT	121	1165
1041909	N/A	N/A	446170	446189	TTCCTCCATCCATCCCCCTA	108	1166
1041941	N/A	N/A	446742	446761	AGCCCATTTTTTCATCCAGT	7	1167
1041973	N/A	N/A	447025	447044	TGTGGCTTTACCGCCTAACA	106	1168
1042005	N/A	N/A	447997	448016	TCTCCTCTTTATACCAGGGA	47	1169
1042037	N/A	N/A	448611	448630	TATTTTTTTACTACCTCCAC	72	1170
1042069	N/A	N/A	448882	448901	AGTGACCACACTATCCGATG	28	1171
1042101	N/A	N/A	449428	449447	CTTGAATTTAAAACCCATAT	83	1172
1042133	N/A	N/A	449745	449764	TGCACACATCTCAAATAGGT	40	1173
1042165	N/A	N/A	450037	450056	TTTGCCTAAATTCTGCCTTT	68	1174
1042197	N/A	N/A	450727	450746	CTCACCAACCTCATCTCTCG	98	1175
1042229	N/A	N/A	451449	451468	ACAACTAACTATATATTGTT	97	1176
1042261	N/A	N/A	451738	451757	GTTTCCCTCTAAAGACTTCA	17	1177
1042293	N/A	N/A	452058	452077	GACCAGAAGCCTTAGTTCCA	26	1178
1042325	N/A	N/A	452384	452403	ACACAGAAACATATATGTGC	87	1179
1042357	N/A	N/A	452669	452688	ATTGGCCCCCAAACCCATTT	83	1180
1042389	N/A	N/A	453547	453566	TCTGAATGAATATTGGCTAT	21	1181
1042421	N/A	N/A	454309	454328	GATGAGAATTAAACTGCTAT	66	1182
1042453	N/A	N/A	455147	455166	GAGTCATACATATAGACTTT	132	1183
1042485	N/A	N/A	455452	455471	TCAGGATACACCAAGGGAGG	82	1184
1042517	N/A	N/A	456712	456731	AACTGCTATTATCATACAGG	57	1185

Table 17

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040086	1112	1131	435831	435850	CCCGGCCACCAGGGTTGCCC	110	1186
1040118	2897	2916	457150	457169	GATACTCTACCAAAACTTCA	64	1187
1040150	3412	3431	457665	457684	CCCACGCTGCCTCTACTTGC	56	1188
1040182	4147	4166	458400	458419	GCACTAGTAAAAAGCAGAAA	72	1189
1040214	4594	4613	458847	458866	GTTTAAAGTGAGATACAGTA	15	1190
1040246	4923	4942	459176	459195	AGGTTCTTTAAAAGTTCATC	12	1191
1040278	5330	5349	459583	459602	GGTTTGTACCAAACATTAAA	106	1192
1040310	5652	5671	459905	459924	TACACCCCAGAAAACGGTTT	124	1193
1040342	6069	6088	460322	460341	CTATTGCTCCAAACCATGTG	39	1194
1040374	6678	6697	460931	460950	ACTGGCCAACACGCTCAGAA	102	1195
1040406	7294	7313	461547	461566	ACCAACATAGAAAATTATCC	30	1196
1040438	7722	7741	461975	461994	AGTAAAGATCAAACTGTGCA	14	1197
1040470	8178	8197	462431	462450	TGGGTTAAAAACAAATGTGG	81	1198
1040502	8484	8503	462737	462756	TCAGCTTCTCAAATCAGGTG	13	1199
1040534	8740	8759	462993	463012	TAGTAATTCTTCCAGGCCAT	23	1200
1040566	9181	9200	463434	463453	TTCTGGCCTCTTTATATTAA	30	1201
1040598	9521	9540	463774	463793	CTTGAGTCCTTTCAGATAAG	28	1202
1040630	10087	10106	464340	464359	TCTGATATTAAAACATCCAG	34	1203
1040662	10290	10309	464543	464562	GCATATGGAAAAAAGTTCTC	24	1204
1040694	10583	10602	464836	464855	TACTGAAACAATAAACTTGT	102	1205
1040726	N/A	N/A	22134	22153	TCTTCCTCCTTTTATATCTG	30	1206
1040758	N/A	N/A	34802	34821	GGATTAAAAATTATGACCTC	57	1207
1040790	N/A	N/A	59689	59708	GGAGCAGTTCCTTAACTATC	20	1208
1040822	N/A	N/A	79548	79567	CCCCTTACCCAAACCCTTGG	124	1209
1040854	N/A	N/A	102583	102602	AGAGATAATTTTTAATGCAG	34	1210
1040886	N/A	N/A	129211	129230	CCATTAAACATTTATTTTGC	11	1211
1040918	N/A	N/A	158178	158197	TCTATATTCCCTTAACCGTA	32	1212
1040950	N/A	N/A	182959	182978	CATTTTCAACCTTATGATAT	42	1213
1040982	N/A	N/A	203492	203511	CAGACATTCCTTTAATATGC	17	1214
1041014	N/A	N/A	218412	218431	TAGAACTTTTAAAGCAAGGC	52	1215
1041046	N/A	N/A	242061	242080	AGTCAAATAGTCTATCAGTA	11	1216
1041078	N/A	N/A	263847	263866	ACATGATTTTAAAAGTCTTA	73	1217
1041110	N/A	N/A	281874	281893	TCCCCACACCCTTAAACTGC	115	1218
1041142	N/A	N/A	310242	310261	TACACATAAATTTATATCTG	78	1219
1041174	N/A	N/A	329490	329509	TGGTTCTATATTTATGTACC	25	1220
1041206	N/A	N/A	353449	353468	TTGTCTAAACCTGTTTGAGG	6	1221
1041238	N/A	N/A	375665	375684	GCTACCAAAATACAGAACTT	66	1222

1041270	N/A	N/A	399709	399728	GCACCATTTTAAAAATGGCT	123	1223
1041302	N/A	N/A	430826	430845	TCATCTAAACCTAATACGGC	99	1224
1041334	N/A	N/A	437968	437987	TCTGTCTTTTCCTGGTAAGA	11	1225
1041366	N/A	N/A	438425	438444	CTGTTGTTTGCCACATTTCC	9	1226
1041398	N/A	N/A	438975	438994	CCAGAGCTAATTCCTAGGAG	4	1227
1041430	N/A	N/A	439288	439307	TTGGGCAGTGAAAGAAATGG	74	1228
1041462	N/A	N/A	439989	440008	ACCTACAGTGACATCTCATA	63	1229
1041494	N/A	N/A	440279	440298	TCTGTTCACAAAAATGTGTT	94	1230
1041526	N/A	N/A	440834	440853	CTCTTTCATTTAATCATTAA	47	1231
1041558	N/A	N/A	441464	441483	TCCCCAATCAAATTTGTGAT	62	1232
1041590	N/A	N/A	441897	441916	GTAGTGGTACACACCCATAG	77	1233
1041622	N/A	N/A	442320	442339	GGCATCTTTCCACAGTCTTA	43	1234
1041654	N/A	N/A	442947	442966	CCGAGCCATCTAAGTTGAAG	30	1235
1041686	N/A	N/A	443225	443244	ATCCAGTTCATACTCAGAAA	29	1236
1041718	N/A	N/A	443659	443678	CACCCACGCCAGGACAGTCG	128	1237
1041750	N/A	N/A	444049	444068	TTCCAGCACCAGAACAGACA	116	1238
1041782	N/A	N/A	444483	444502	TCTGTATAATAATGTAATGC	11	1239
1041814	N/A	N/A	445371	445390	GTTCTATTTAAAACACTGAA	25	1240
1041846	N/A	N/A	445703	445722	CATACAAATTTCGCCTGTTG	55	1241
1041878	N/A	N/A	445947	445966	ACTACTATATCTAAACACTA	109	1242
1041910	N/A	N/A	446176	446195	TACCCCTTCCTCCATCCATC	88	1243
1041942	N/A	N/A	446750	446769	CTCAATATAGCCCATTTTTT	47	1244
1041974	N/A	N/A	447063	447082	GACCTCCCCCAGGGAGAGGA	75	1245
1042006	N/A	N/A	447998	448017	TTCTCCTCTTTATACCAGGG	12	1246
1042038	N/A	N/A	448613	448632	ACTATTTTTTTACTACCTCC	54	1247
1042070	N/A	N/A	448885	448904	ACCAGTGACCACACTATCCG	45	1248
1042102	N/A	N/A	449429	449448	CCTTGAATTTAAAACCCATA	42	1249
1042134	N/A	N/A	449762	449781	GAAAGTTAAAATCTTGTTGC	57	1250
1042166	N/A	N/A	450040	450059	CTTTTTGCCTAAATTCTGCC	70	1251
1042198	N/A	N/A	450728	450747	TCTCACCAACCTCATCTCTC	77	1252
1042230	N/A	N/A	451450	451469	AACAACTAACTATATATTGT	112	1253
1042262	N/A	N/A	451767	451786	AGTGCAAAAGTCAGGATACA	12	1254
1042294	N/A	N/A	452064	452083	TCAGAAGACCAGAAGCCTTA	62	1255
1042326	N/A	N/A	452397	452416	ACATTTACATCACACACAGA	104	1256
1042358	N/A	N/A	452685	452704	GGATTTTATCCCAGTCATTG	57	1257
1042390	N/A	N/A	453577	453596	GAGGAATGAAAATGGTAGAT	25	1258
1042422	N/A	N/A	454311	454330	CAGATGAGAATTAAACTGCT	62	1259
1042454	N/A	N/A	455148	455167	AGAGTCATACATATAGACTT	129	1260
1042486	N/A	N/A	455459	455478	ATGGAGTTCAGGATACACCA	54	1261
1042518	N/A	N/A	456740	456759	GGTCTTAGATTTTATGAGCT	16	1262

Table 18

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040087	1115	1134	435834	435853	GGCCCCGGCCACCAGGGTTG	104	1263
1040119	2898	2917	457151	457170	GGATACTCTACCAAAACTTC	20	1264
1040151	3423	3442	457676	457695	GTTTCCTTTCCCCCACGCTG	23	1265
1040183	4148	4167	458401	458420	TGCACTAGTAAAAAGCAGAA	99	1266
1040215	4609	4628	458862	458881	TTTTTTCCCCAAAGAGTTTA	37	1267
1040247	4924	4943	459177	459196	AAGGTTCTTTAAAAGTTCAT	20	1268
1040279	5332	5351	459585	459604	TGGGTTTGTACCAAACATTA	59	1269
1040311	5676	5695	459929	459948	CTAAACCTATTCAAATGTTT	90	1270
1040343	6078	6097	460331	460350	ATGATGTTCCTATTGCTCCA	11	1271
1040375	6750	6769	461003	461022	TCTTCCTATTTGAAGAGAAA	64	1272
1040407	7311	7330	461564	461583	GGGAAAACGAAAAGTTGACC	29	1273
1040439	7724	7743	461977	461996	TCAGTAAAGATCAAACTGTG	103	1274
1040471	8180	8199	462433	462452	TCTGGGTTAAAAACAAATGT	69	1275
1040503	8486	8505	462739	462758	CTTCAGCTTCTCAAATCAGG	26	1276
1040535	8767	8786	463020	463039	ATAGGTATAGTTTAAGAGCC	22	1277
1040567	9195	9214	463448	463467	ATGCTCCGTATTTATTCTGG	9	1278
1040599	9523	9542	463776	463795	GACTTGAGTCCTTTCAGATA	32	1279
1040631	10088	10107	464341	464360	ATCTGATATTAAAACATCCA	33	1280
1040663	10327	10346	464580	464599	TACAATATTTTACACTGGAA	11	1281
1040695	10609	10628	464862	464881	GCACTGTTATTTTATTAGTA	41	1282
1040727	N/A	N/A	22675	22694	CTGTGGTTTTAAAGGCTGTA	4	1283
1040759	N/A	N/A	34869	34888	GGTTTTAAAAACATCCTCCT	41	1284
1040791	N/A	N/A	63051	63070	TTTTAGCACCTTTAAACTCT	85	1285
1040823	N/A	N/A	79759	79778	CTCTCATTTTAAAGTTTTCT	44	1286
1040855	N/A	N/A	103256	103275	ATCTTTATTCAAAAATGCAA	88	1287
1040887	N/A	N/A	132848	132867	TTCATGTTTTAAAGCTGAGA	11	1288
1040919	N/A	N/A	158451	158470	CTCACAATTCAAAATTATTC	44	1289
1040951	N/A	N/A	182994	183013	AACCTTAGAAATGTACATTT	29	1290
1040983	N/A	N/A	204258	204277	CTAGCAATTCAAAACAATAT	45	1291
1041015	N/A	N/A	219043	219062	CTTCTCCTTCCTTAATAGAT	65	1292
1041047	N/A	N/A	243398	243417	TCTCAAGGCCCTTAATTGCC	67	1293
1041079	N/A	N/A	264140	264159	ACTTTTAAATCCCCCTAAAG	105	1294
1041111	N/A	N/A	281939	281958	CTCACATTTCTTTATACACA	2	1295
1041143	N/A	N/A	311352	311371	GTGAGATTTTAAAGACATTC	1	1296
1041175	N/A	N/A	330016	330035	GATGCCAAACTATTATCTCA	7	1297
1041207	N/A	N/A	354249	354268	AGACAATTTTAAAAGCTTCC	8	1298
1041239	N/A	N/A	375816	375835	TCTCTTAACCAAAGAATCTG	132	1299
1041271	N/A	N/A	400962	400981	ATGCTGTTCCTTTATAACGG	16	1300

1041303	N/A	N/A	431185	431204	AATTTCTAAATTTAGCCCAG	55	1301
1041335	N/A	N/A	437990	438009	TCCCCTCACTCCAACGGCAT	80	1302
1041367	N/A	N/A	438448	438467	CTCCCATGAAACCACAATAA	142	1303
1041399	N/A	N/A	439002	439021	CTGACTTTTATATGCAAACC	25	1304
1041431	N/A	N/A	439344	439363	CTCGATAGCCAGGAAAGCTC	64	1305
1041463	N/A	N/A	439996	440015	ACTGTAAACCTACAGTGACA	130	1306
1041495	N/A	N/A	440280	440299	CTCTGTTCACAAAAATGTGT	95	1307
1041527	N/A	N/A	440836	440855	TTCTCTTTCATTTAATCATT	16	1308
1041559	N/A	N/A	441465	441484	TTCCCCAATCAAATTTGTGA	83	1309
1041591	N/A	N/A	442071	442090	GAGATTATCTCCTATGAAGA	50	1310
1041623	N/A	N/A	442374	442393	AGCATTTTTCTCCTACATTG	14	1311
1041655	N/A	N/A	442950	442969	GGCCCGAGCCATCTAAGTTG	129	1312
1041687	N/A	N/A	443226	443245	AATCCAGTTCATACTCAGAA	47	1313
1041719	N/A	N/A	443664	443683	ACTCACACCCACGCCAGGAC	109	1314
1041751	N/A	N/A	444094	444113	CCACAAACAAAAATGTGGTT	79	1315
1041783	N/A	N/A	444487	444506	CTGTTCTGTATAATAATGTA	48	1316
1041815	N/A	N/A	445372	445391	TGTTCTATTTAAAACACTGA	62	1317
1041847	N/A	N/A	445705	445724	GACATACAAATTTCGCCTGT	22	1318
1041879	N/A	N/A	445948	445967	AACTACTATATCTAAACACT	95	1319
1041911	N/A	N/A	446181	446200	CTGCCTACCCCTTCCTCCAT	80	1320
1041943	N/A	N/A	446755	446774	GACAGCTCAATATAGCCCAT	28	1321
1041975	N/A	N/A	447085	447104	AGCCAGAACTAAAGTGGGCT	74	1322
1042007	N/A	N/A	448000	448019	CCTTCTCCTCTTTATACCAG	35	1323
1042039	N/A	N/A	448615	448634	ATACTATTTTTTTACTACCT	65	1324
1042071	N/A	N/A	448888	448907	GACACCAGTGACCACACTAT	46	1325
1042103	N/A	N/A	449430	449449	TCCTTGAATTTAAAACCCAT	55	1326
1042135	N/A	N/A	449763	449782	TGAAAGTTAAAATCTTGTTG	75	1327
1042167	N/A	N/A	450041	450060	TCTTTTTGCCTAAATTCTGC	43	1328
1042199	N/A	N/A	450731	450750	TCCTCTCACCAACCTCATCT	77	1329
1042231	N/A	N/A	451490	451509	CTTTTAGAAACTAACTCTGG	107	1330
1042263	N/A	N/A	451782	451801	GTACTATAATTGATTAGTGC	50	1331
1042295	N/A	N/A	452071	452090	GTGACATTCAGAAGACCAGA	15	1332
1042327	N/A	N/A	452400	452419	ACTACATTTACATCACACAC	83	1333
1042359	N/A	N/A	452688	452707	TTAGGATTTTATCCCAGTCA	28	1334
1042391	N/A	N/A	453658	453677	GCATTATAGAAAATACTAAA	85	1335
1042423	N/A	N/A	454312	454331	GCAGATGAGAATTAAACTGC	100	1336
1042455	N/A	N/A	455154	455173	TCATATAGAGTCATACATAT	45	1337
1042487	N/A	N/A	455532	455551	TGAACATTCCAAAGTGGAGC	44	1338
1042519	N/A	N/A	456742	456761	GCGGTCTTAGATTTTATGAG	24	1339

Table 19

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040088	1144	1163	435863	435882	CCCTGCCGGCCCATGCCTCC	159	1340
1040120	2908	2927	457161	457180	CACAAAAAAAGGATACTCTA	104	1341
1040152	3453	3472	457706	457725	ATCTGGATACAAATGATAAG	50	1342
1040184	4176	4195	458429	458448	GTCCACCACAACACCCTGGT	78	1343
1040216	4671	4690	458924	458943	CAGAGCTGAAATGTAGTTAC	12	1344
1040248	4926	4945	459179	459198	GCAAGGTTCTTTAAAAGTTC	11	1345
1040280	5347	5366	459600	459619	ATGAAATACCCTTTCTGGGT	124	1346
1040312	5684	5703	459937	459956	TAGCTATTCTAAACCTATTC	140	1347
1040344	6080	6099	460333	460352	TGATGATGTTCCTATTGCTC	15	1348
1040376	6870	6889	461123	461142	GAAGAATTTCTACCCCTGTC	39	1349
1040408	7336	7355	461589	461608	ATCCCAAACTAAACTGGGTG	105	1350
1040440	7732	7751	461985	462004	AACATATTTCAGTAAAGATC	13	1351
1040472	8194	8213	462447	462466	TCTATTTCAGAAATTCTGGG	11	1352
1040504	8505	8524	462758	462777	TGCTTCAAAATTTTGTTTTC	40	1353
1040536	8815	8834	463068	463087	TTCCCCTCCCTCAGACGAGG	109	1354
1040568	9206	9225	463459	463478	ATTCTGAGAAGATGCTCCGT	35	1355
1040600	9525	9544	463778	463797	AAGACTTGAGTCCTTTCAGA	26	1356
1040632	10089	10108	464342	464361	GATCTGATATTAAAACATCC	20	1357
1040664	10329	10348	464582	464601	AGTACAATATTTTACACTGG	14	1358
1040696	N/A	N/A	5825	5844	GTCAAGTTTTAAAATGTGAC	68	1359
1040728	N/A	N/A	22774	22793	ACTGAAACAATTTATCTAAG	83	1360
1040760	N/A	N/A	36098	36117	ACAAAAATAATTTAAGCCAC	106	1361
1040792	N/A	N/A	63073	63092	TACTATCACCTTTAAACTTT	71	1362
1040824	N/A	N/A	80953	80972	ACCGCCAAAACCAACCAGGG	65	1363
1040856	N/A	N/A	103405	103424	CTAATCTATCAAATAAAGGA	105	1364
1040888	N/A	N/A	133117	133136	GAGAGGTTTCATTATGTAAA	5	1365
1040920	N/A	N/A	158507	158526	GCACTTAGACAATGCTGCAG	106	1366
1040952	N/A	N/A	183278	183297	GGTAAGTTATTTTAAAACTT	76	1367
1040984	N/A	N/A	205648	205667	AGTTTTACGATATATGAATC	81	1368
1041016	N/A	N/A	219199	219218	TACCATTATTTTTAGCTTTT	18	1369
1041048	N/A	N/A	243460	243479	CAGTTTATTCTTTACCCAAA	10	1370
1041080	N/A	N/A	264569	264588	CCCACATTTTAAAGATGCAG	46	1371
1041112	N/A	N/A	282392	282411	TCCAGAAACCTTTATTATTG	1	1372
1041144	N/A	N/A	311667	311686	AACAGGTTACAAATACGGTT	1	1373
1041176	N/A	N/A	330322	330341	ATTCTGTTTTAAATTCCTTT	1	1374
1041208	N/A	N/A	354293	354312	ATGCAATTTCAAAAGCTGGC	10	1375
1041240	N/A	N/A	376063	376082	GTGGATACTTTTTAAAACTC	2	1376
1041272	N/A	N/A	401167	401186	GTCGCAAACCTTTATGGAGT	6	1377

1041304	N/A	N/A	431998	432017	CAAATCCAAATTTATTCTTC	76	1378
1041336	N/A	N/A	437997	438016	CATCTAATCCCCTCACTCCA	92	1379
1041368	N/A	N/A	438450	438469	GCCTCCCATGAAACCACAAT	122	1380
1041400	N/A	N/A	439003	439022	CCTGACTTTTATATGCAAAC	11	1381
1041432	N/A	N/A	439351	439370	AAGTACGCTCGATAGCCAGG	22	1382
1041464	N/A	N/A	439999	440018	AAGACTGTAAACCTACAGTG	101	1383
1041496	N/A	N/A	440281	440300	CCTCTGTTCACAAAAATGTG	121	1384
1041528	N/A	N/A	440838	440857	ATTTCTCTTTCATTTAATCA	33	1385
1041560	N/A	N/A	441466	441485	CTTCCCCAATCAAATTTGTG	87	1386
1041592	N/A	N/A	442072	442091	AGAGATTATCTCCTATGAAG	70	1387
1041624	N/A	N/A	442397	442416	AGGGATAGTGACAAACACGG	8	1388
1041656	N/A	N/A	442952	442971	AGGGCCCGAGCCATCTAAGT	122	1389
1041688	N/A	N/A	443233	443252	CCCCTCAAATCCAGTTCATA	111	1390
1041720	N/A	N/A	443705	443724	CATCATGATAACAACTGCTG	47	1391
1041752	N/A	N/A	444095	444114	CCCACAAACAAAAATGTGGT	100	1392
1041784	N/A	N/A	444575	444594	GAGTAAAATGATCAGTGGGT	15	1393
1041816	N/A	N/A	445373	445392	GTGTTCTATTTAAAACACTG	107	1394
1041848	N/A	N/A	445706	445725	AGACATACAAATTTCGCCTG	45	1395
1041880	N/A	N/A	445954	445973	GTCAATAACTACTATATCTA	54	1396
1041912	N/A	N/A	446182	446201	TCTGCCTACCCCTTCCTCCA	61	1397
1041944	N/A	N/A	446788	446807	CCACAGATAACCAAAGCACG	37	1398
1041976	N/A	N/A	447087	447106	CCAGCCAGAACTAAAGTGGG	75	1399
1042008	N/A	N/A	448004	448023	GGCCCCTTCTCCTCTTTATA	118	1400
1042040	N/A	N/A	448617	448636	TGATACTATTTTTTTACTAC	97	1401
1042072	N/A	N/A	448922	448941	GAGACAGAACATACACGCAA	35	1402
1042104	N/A	N/A	449432	449451	ATTCCTTGAATTTAAAACCC	51	1403
1042136	N/A	N/A	449764	449783	GTGAAAGTTAAAATCTTGTT	47	1404
1042168	N/A	N/A	450045	450064	TGTTTCTTTTTGCCTAAATT	13	1405
1042200	N/A	N/A	450734	450753	TTTTCCTCTCACCAACCTCA	67	1406
1042232	N/A	N/A	451491	451510	ACTTTTAGAAACTAACTCTG	71	1407
1042264	N/A	N/A	451796	451815	GCCCTTTATAACAGGTACTA	44	1408
1042296	N/A	N/A	452072	452091	TGTGACATTCAGAAGACCAG	27	1409
1042328	N/A	N/A	452405	452424	TCAAAACTACATTTACATCA	118	1410
1042360	N/A	N/A	452691	452710	GGTTTAGGATTTTATCCCAG	25	1411
1042392	N/A	N/A	453659	453678	TGCATTATAGAAAATACTAA	121	1412
1042424	N/A	N/A	454313	454332	GGCAGATGAGAATTAAACTG	38	1413
1042456	N/A	N/A	455163	455182	CAGGGCTTCTCATATAGAGT	31	1414
1042488	N/A	N/A	455538	455557	GGCACTTGAACATTCCAAAG	10	1415
1042520	N/A	N/A	456757	456776	GCTCACAAGCCCAGCGCGGT	90	1416

Table 20

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040089	1170	1189	435889	435908	TGTTGTAAACCAAGCTCCAC	56	1417
1040121	2915	2934	457168	457187	GTCCAAACACAAAAAAAGGA	90	1418
1040153	3475	3494	457728	457747	TATTTTAGCCTACAGTACAG	70	1419
1040185	4179	4198	458432	458451	CCTGTCCACCACAACACCCT	80	1420
1040217	4683	4702	458936	458955	TCAGCAATTCTGCAGAGCTG	103	1421
1040249	4953	4972	459206	459225	AAGTTATAAACTCAATATGT	38	1422
1040281	5348	5367	459601	459620	TATGAAATACCCTTTCTGGG	106	1423
1040313	5686	5705	459939	459958	TCTAGCTATTCTAAACCTAT	80	1424
1040345	6092	6111	460345	460364	CCACAAAAATTATGATGATG	45	1425
1040377	6871	6890	461124	461143	CGAAGAATTTCTACCCCTGT	47	1426
1040409	7338	7357	461591	461610	TCATCCCAAACTAAACTGGG	87	1427
1040441	7734	7753	461987	462006	GCAACATATTTCAGTAAAGA	13	1428
1040473	8203	8222	462456	462475	CTTAAATTCTCTATTTCAGA	30	1429
1040505	8506	8525	462759	462778	GTGCTTCAAAATTTTGTTTT	27	1430
1040537	8821	8840	463074	463093	ACCGAGTTCCCCTCCCTCAG	106	1431
1040569	9217	9236	463470	463489	ACAGGAATACTATTCTGAGA	38	1432
1040601	9550	9569	463803	463822	GAAGCCTCCAATGTATCTGC	17	1433
1040633	10134	10153	464387	464406	GGTGTCTGTTTTCCCTTGGC	14	1434
1040665	10330	10349	464583	464602	AAGTACAATATTTTACACTG	20	1435
1040697	N/A	N/A	6321	6340	GGCCATAAAATTGTAAACTG	44	1436
1040729	N/A	N/A	23146	23165	AACATCTAAATTTATAATGA	113	1437
1040761	N/A	N/A	36881	36900	AGGTGGTTACAAACATAAAT	35	1438
1040793	N/A	N/A	63098	63117	AGCTAAAAACCCAACATGGG	81	1439
1040825	N/A	N/A	81039	81058	GACAGTTATTTTTAAGAGGC	7	1440
1040857	N/A	N/A	103451	103470	TTGGACTTTTAAATGTAAGT	83	1441
1040889	N/A	N/A	135046	135065	TGTGTCTAAATTTATGGTAG	13	1442
1040921	N/A	N/A	160360	160379	GTTGAATTTCAAAAATCAAA	59	1443
1040953	N/A	N/A	184290	184309	CAGGAAAAAATACAGGGTGT	19	1444
1040985	N/A	N/A	206209	206228	ACCTAAAAAAAATATAGATCC	142	1445
1041017	N/A	N/A	223097	223116	CTAATTAATCCTTAAATTGC	109	1446
1041049	N/A	N/A	244961	244980	TTTCAATATATTTACACACT	63	1447
1041081	N/A	N/A	266459	266478	CTCACACAAATTTACATTCT	89	1448
1041113	N/A	N/A	284256	284275	ACCTAAAAAATACATCTTTA	94	1449
1041145	N/A	N/A	313344	313363	CTGAAGATTCCTTAATATCT	1	1450
1041177	N/A	N/A	331091	331110	CTAATGTTTTAAAACTCTTG	35	1451
1041209	N/A	N/A	355246	355265	TTCCAATTTTAAAAAACCTG	44	1452
1041241	N/A	N/A	376190	376209	CTGTCAAAAATATAATACCT	81	1453
1041273	N/A	N/A	401168	401187	TGTCGCAAACCTTTATGGAG	33	1454

1041305	N/A	N/A	432296	432315	AAGTCCTTTCAAAGCCAAGT	38	1455
1041337	N/A	N/A	437999	438018	AGCATCTAATCCCCTCACTC	42	1456
1041369	N/A	N/A	438464	438483	AACCCGTTTACCCTGCCTCC	77	1457
1041401	N/A	N/A	439004	439023	GCCTGACTTTTATATGCAAA	13	1458
1041433	N/A	N/A	439362	439381	ACACTTGTAGAAAGTACGCT	8	1459
1041465	N/A	N/A	440005	440024	CTTCCAAAGACTGTAAACCT	65	1460
1041497	N/A	N/A	440282	440301	GCCTCTGTTCACAAAAATGT	99	1461
1041529	N/A	N/A	440844	440863	AAGCCAATTTCTCTTTCATT	57	1462
1041561	N/A	N/A	441471	441490	CACAACTTCCCCAATCAAAT	70	1463
1041593	N/A	N/A	442076	442095	CTCAAGAGATTATCTCCTAT	30	1464
1041625	N/A	N/A	442399	442418	ACAGGGATAGTGACAAACAC	24	1465
1041657	N/A	N/A	442969	442988	CTGTGAATCACTTTCTCAGG	73	1466
1041689	N/A	N/A	443234	443253	ACCCCTCAAATCCAGTTCAT	129	1467
1041721	N/A	N/A	443723	443742	GTAGACAGCCAGTAAGTACA	62	1468
1041753	N/A	N/A	444096	444115	ACCCACAAACAAAAATGTGG	132	1469
1041785	N/A	N/A	444648	444667	CGCCAATGTGAAAAGGCGAC		1470
1041817	N/A	N/A	445374	445393	AGTGTTCTATTTAAAACACT	131	1471
1041849	N/A	N/A	445708	445727	CCAGACATACAAATTTCGCC	40	1472
1041881	N/A	N/A	445955	445974	AGTCAATAACTACTATATCT	46	1473
1041913	N/A	N/A	446221	446240	CCAGCAAGCCCATGTGCTCA	109	1474
1041945	N/A	N/A	446792	446811	AGTACCACAGATAACCAAAG	52	1475
1041977	N/A	N/A	447180	447199	CTGTATGGAAAAACATTGCA	29	1476
1042009	N/A	N/A	448133	448152	ATGATGATCATTATGTAGAG	24	1477
1042041	N/A	N/A	448619	448638	AATGATACTATTTTTTTACT	77	1478
1042073	N/A	N/A	448923	448942	GGAGACAGAACATACACGCA	44	1479
1042105	N/A	N/A	449439	449458	TCTGTGAATTCCTTGAATTT	41	1480
1042137	N/A	N/A	449765	449784	GGTGAAAGTTAAAATCTTGT	60	1481
1042169	N/A	N/A	450072	450091	TCTTTAATCACTTCAAAGGC	54	1482
1042201	N/A	N/A	450754	450773	GGCTTTCCCAATAAACCTGC	37	1483
1042233	N/A	N/A	451493	451512	GTACTTTTAGAAACTAACTC	47	1484
1042265	N/A	N/A	451798	451817	AAGCCCTTTATAACAGGTAC	38	1485
1042297	N/A	N/A	452094	452113	GCCCAACACCAGGCAGAGGT	82	1486
1042329	N/A	N/A	452407	452426	TTTCAAAACTACATTTACAT	117	1487
1042361	N/A	N/A	452759	452778	TTGTAAATTTTACGAATAGT	63	1488
1042393	N/A	N/A	453673	453692	ACCATCAACAGATCTGCATT	62	1489
1042425	N/A	N/A	454359	454378	GCCTAGCCCCAAACAGGAAA	117	1490
1042457	N/A	N/A	455172	455191	AGGATGCACCAGGGCTTCTC	79	1491
1042489	N/A	N/A	455557	455576	GGGCCTGTTTTCTCCTGAAG	116	1492
1042521	N/A	N/A	456758	456777	GGCTCACAAGCCCAGCGCGG	132	1493

Table 21

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040090	1171	1190	435890	435909	CTGTTGTAAACCAAGCTCCA	64	1494
1040122	2927	2946	457180	457199	ATGACCAGCCCTGTCCAAAC	73	1495
1040154	3482	3501	457735	457754	ACTGTGTTATTTTAGCCTAC	11	1496
1040186	4224	4243	458477	458496	CCCAACCCCCCTTACCCCAT	82	1497
1040218	4709	4728	458962	458981	CATTGAAACTTTCAATATCT	43	1498
1040250	4967	4986	459220	459239	CAGGAATATCACACAAGTTA	17	1499
1040282	5349	5368	459602	459621	CTATGAAATACCCTTTCTGG	79	1500
1040314	5687	5706	459940	459959	TTCTAGCTATTCTAAACCTA	75	1501
1040346	6094	6113	460347	460366	AACCACAAAAATTATGATGA	59	1502
1040378	6872	6891	461125	461144	CCGAAGAATTTCTACCCCTG	31	1503
1040410	7339	7358	461592	461611	ATCATCCCAAACTAAACTGG	71	1504
1040442	7739	7758	461992	462011	TTTTGGCAACATATTTCAGT	16	1505
1040474	8207	8226	462460	462479	TGTTCTTAAATTCTCTATTT	18	1506
1040506	8508	8527	462761	462780	GAGTGCTTCAAAATTTTGTT	20	1507
1040538	8843	8862	463096	463115	CAGTATTCTCAAATCGCAGA	58	1508
1040570	9219	9238	463472	463491	GGACAGGAATACTATTCTGA	45	1509
1040602	9554	9573	463807	463826	GGGTGAAGCCTCCAATGTAT	29	1510
1040634	10151	10170	464404	464423	CCCTCAACCCAAGTTCTGGT	78	1511
1040666	10332	10351	464585	464604	GCAAGTACAATATTTTACAC	13	1512
1040698	N/A	N/A	6643	6662	CACTGAAAAATATATGTTCA	28	1513
1040730	N/A	N/A	23318	23337	CACTATAAAAACATCTAACA	98	1514
1040762	N/A	N/A	38292	38311	TTCAACAATATTTATGCCCA	5	1515
1040794	N/A	N/A	63099	63118	CAGCTAAAAACCCAACATGG	109	1516
1040826	N/A	N/A	81067	81086	AGTTATATATTTTAGCTGAA	58	1517
1040858	N/A	N/A	103630	103649	GCTATATTTTAAAAAGGATC	89	1518
1040890	N/A	N/A	137052	137071	CTTTCATTTCAAACTTACTG	59	1519
1040922	N/A	N/A	161567	161586	ACTTTCTTTTAAATTCTAAC	69	1520
1040954	N/A	N/A	184602	184621	GATGGTAATTTTTAGAGGTG	4	1521
1040986	N/A	N/A	206522	206541	TCTTTCTATATTTATCTATA	51	1522
1041018	N/A	N/A	223242	223261	GTTTACAAAATATTTGCACA	37	1523
1041050	N/A	N/A	245286	245305	TCTATCAAACCTAATCTATC	53	1524
1041082	N/A	N/A	267260	267279	AAGGAATTTCTTTACACCAT	27	1525
1041114	N/A	N/A	284274	284293	GCACTTCGAATTTATACCAC	2	1526
1041146	N/A	N/A	314135	314154	AACATAAAAAATATACCTAA	109	1527
1041178	N/A	N/A	331394	331413	GCTGTTAAAATATGCTTTCC	2	1528
1041210	N/A	N/A	356766	356785	GGGCACTACCCTTATCTTAA	38	1529
1041242	N/A	N/A	376191	376210	CCTGTCAAAAATATAATACC	89	1530
1041274	N/A	N/A	402544	402563	CCTTTAAAAATATGCCTTTT	46	1531

1041306	N/A	N/A	432451	432470	CCAATAAAACCCCACAGGGT	109	1532
1041338	N/A	N/A	438003	438022	CTTTAGCATCTAATCCCCTC	59	1533
1041370	N/A	N/A	438465	438484	AAACCCGTTTACCCTGCCTC	76	1534
1041402	N/A	N/A	439005	439024	GGCCTGACTTTTATATGCAA	117	1535
1041434	N/A	N/A	439383	439402	GTTTTCAAATCCTAGATGGA	26	1536
1041466	N/A	N/A	440010	440029	GGGCCCTTCCAAAGACTGTA	124	1537
1041498	N/A	N/A	440298	440317	ACCTCTTTTCACACCTGCCT	22	1538
1041530	N/A	N/A	440851	440870	CACAGGGAAGCCAATTTCTC	76	1539
1041562	N/A	N/A	441483	441502	CATCTCTTCTTCCACAACTT	52	1540
1041594	N/A	N/A	442078	442097	CTCTCAAGAGATTATCTCCT	104	1541
1041626	N/A	N/A	442489	442508	CTTTCCTCCCACAGCACCTA	49	1542
1041658	N/A	N/A	442983	443002	GATTTATTTTTCAGCTGTGA	6	1543
1041690	N/A	N/A	443237	443256	TGCACCCCTCAAATCCAGTT	99	1544
1041722	N/A	N/A	443729	443748	CCATCGGTAGACAGCCAGTA	39	1545
1041754	N/A	N/A	444105	444124	GGTACAAAGACCCACAAACA	51	1546
1041786	N/A	N/A	444737	444756	AACATAATATTCAGTGCTAA	40	1547
1041818	N/A	N/A	445375	445394	GAGTGTTCTATTTAAAACAC	82	1548
1041850	N/A	N/A	445710	445729	TCCCAGACATACAAATTTCG	90	1549
1041882	N/A	N/A	445956	445975	TAGTCAATAACTACTATATC	148	1550
1041914	N/A	N/A	446222	446241	GCCAGCAAGCCCATGTGCTC	121	1551
1041946	N/A	N/A	446793	446812	CAGTACCACAGATAACCAAA	30	1552
1041978	N/A	N/A	447541	447560	GCTCAGTTAAAATCTGAAAG	38	1553
1042010	N/A	N/A	448228	448247	GTGGGCTCAAGATATCTTCC	113	1554
1042042	N/A	N/A	448621	448640	AGAATGATACTATTTTTTA	92	1555
1042074	N/A	N/A	448934	448953	GCCTCCCACCAGGAGACAGA	115	1556
1042106	N/A	N/A	449466	449485	GATGTCATCTTCAACTGGAA	28	1557
1042138	N/A	N/A	449771	449790	TTCTTTGGTGAAAGTTAAAA	91	1558
1042170	N/A	N/A	450076	450095	TTCTTCTTTAATCACTTCAA	35	1559
1042202	N/A	N/A	450757	450776	TCTGGCTTTCCCAATAAACC	62	1560
1042234	N/A	N/A	451505	451524	AACAACAATCATGTACTTTT	36	1561
1042266	N/A	N/A	451800	451819	ACAAGCCCTTTATAACAGGT	16	1562
1042298	N/A	N/A	452096	452115	TTGCCCAACACCAGGCAGAG	104	1563
1042330	N/A	N/A	452408	452427	GTTTCAAAACTACATTTACA	100	1564
1042362	N/A	N/A	452769	452788	TCTTCCAATTTTGTAAATTT	35	1565
1042394	N/A	N/A	453674	453693	CACCATCAACAGATCTGCAT	88	1566
1042426	N/A	N/A	454361	454380	AGGCCTAGCCCCAAACAGGA	145	1567
1042458	N/A	N/A	455185	455204	CAGATCTTAAAAAAGGATGC	59	1568
1042490	N/A	N/A	455600	455619	ATCAGGAAAAGATGATGGCC	111	1569
1042522	N/A	N/A	456802	456821	AGAGCACCCACTTAGCTTTC	98	1570

Table 22

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040091	1181	1200	435900	435919	AACCTATTCCCTGTTGTAAA	23	1571
1040123	2969	2988	457222	457241	ACGGCAAATCAAAGAGCTGG	130	1572
1040155	3517	3536	457770	457789	ACAGAAACCTAAAATTAAGA	116	1573
1040187	4227	4246	458480	458499	ACCCCCAACCCCCCTTACCC	102	1574
1040219	4720	4739	458973	458992	CCTTTAAACCACATTGAAAC	69	1575
1040251	4968	4987	459221	459240	GCAGGAATATCACACAAGTT	14	1576
1040283	5351	5370	459604	459623	AACTATGAAATACCCTTTCT	130	1577
1040315	5696	5715	459949	459968	AAGGAACTATTCTAGCTATT	43	1578
1040347	6097	6116	460350	460369	TAGAACCACAAAAATTATGA	65	1579
1040379	6873	6892	461126	461145	ACCGAAGAATTTCTACCCCT	37	1580
1040411	7351	7370	461604	461623	AACAGAAATCAAATCATCCC	58	1581
1040443	7751	7770	462004	462023	AACAAAAATAAATTTTGGCA	103	1582
1040475	8210	8229	462463	462482	ATGTGTTCTTAAATTCTCTA	9	1583
1040507	8523	8542	462776	462795	TGTACTCCTCAAAGTGAGTG	126	1584
1040539	8844	8863	463097	463116	ACAGTATTCTCAAATCGCAG	67	1585
1040571	9251	9270	463504	463523	CTGTCCAGTTTCCACTGTCC	31	1586
1040603	9584	9603	463837	463856	CAGCAAACAAACTAAAGGGA	29	1587
1040635	10152	10171	464405	464424	GCCCTCAACCCAAGTTCTGG	129	1588
1040667	10375	10394	464628	464647	TATGAATTCTTCCATTTTTT	92	1589
1040699	N/A	N/A	7015	7034	AACATTATTCAAAGAAATGT	108	1590
1040731	N/A	N/A	24365	24384	AGGCAGAACATTTAACATCG	29	1591
1040763	N/A	N/A	38732	38751	TCTGTGTTTATTTAGGTTTC	3	1592
1040795	N/A	N/A	64787	64806	ACTGCATTTCAAAACCTACA	25	1593
1040827	N/A	N/A	81310	81329	TTGAAGTTTTAAAGTACATG	87	1594
1040859	N/A	N/A	105462	105481	ATGTTTAAAATATGCATGCC	152	1595
1040891	N/A	N/A	137270	137289	TTTCTCAGAATATAACTGTA	44	1596
1040923	N/A	N/A	162773	162792	GTGTAATTTCAAAATAGGGT	10	1597
1040955	N/A	N/A	185622	185641	AGCTTTCAAATTTATCCACT	9	1598
1040987	N/A	N/A	207222	207241	ACTTAGCCAATTTAACTGCA	26	1599
1041019	N/A	N/A	224367	224386	TCTTTAAAACTATTAGTCAC	81	1600
1041051	N/A	N/A	245290	245309	CTAATCTATCAAACCTAATC	142	1601
1041083	N/A	N/A	267301	267320	TCAGTTAAAATACCTGATGA	94	1602
1041115	N/A	N/A	284506	284525	GGTTAATATTTTTATGGTAT	1	1603
1041147	N/A	N/A	314443	314462	GTTATAATTTAAAAAGTGTT	100	1604
1041179	N/A	N/A	332631	332650	CCGTTTTATTTTTAAACTCG	9	1605
1041211	N/A	N/A	356791	356810	GCTTCATTTTAAAAGATTGT	7	1606
1041243	N/A	N/A	376226	376245	CCACATAAAATATCGAATCA	40	1607
1041275	N/A	N/A	407589	407608	CAGGGCTGTATTTAATTCTG	14	1608

1041307	N/A	N/A	433208	433227	GTTCTCAATCCTTAATGATT	55	1609
1041339	N/A	N/A	438044	438063	GACATATTTTAAAACATGGA	13	1610
1041371	N/A	N/A	438475	438494	AACCAATCCTAAACCCGTTT	62	1611
1041403	N/A	N/A	439006	439025	AGGCCTGACTTTTATATGCA	137	1612
1041435	N/A	N/A	439384	439403	TGTTTTCAAATCCTAGATGG	43	1613
1041467	N/A	N/A	440042	440061	TTTTAAATAAGATCTTTGGG	62	1614
1041499	N/A	N/A	440299	440318	AACCTCTTTTCACACCTGCC	26	1615
1041531	N/A	N/A	440909	440928	AGTAGAGAGATTTAGTGATC	16	1616
1041563	N/A	N/A	441492	441511	GGAGAAAACCATCTCTTCTT	76	1617
1041595	N/A	N/A	442096	442115	GCATTAAAAAACGGAACCCT	103	1618
1041627	N/A	N/A	442494	442513	TTCCCCTTTCCTCCCACAGC	99	1619
1041659	N/A	N/A	442984	443003	TGATTTATTTTTCAGCTGTG	5	1620
1041691	N/A	N/A	443239	443258	AATGCACCCCTCAAATCCAG	109	1621
1041723	N/A	N/A	443762	443781	AGTCAACCAAAAAATAGTAG	40	1622
1041755	N/A	N/A	444110	444129	AGAGAGGTACAAAGACCCAC	52	1623
1041787	N/A	N/A	444740	444759	AACAACATAATATTCAGTGC	27	1624
1041819	N/A	N/A	445394	445413	TGAGTGTAAGAATCTCTGTG	119	1625
1041851	N/A	N/A	445716	445735	ACACTATCCCAGACATACAA	57	1626
1041883	N/A	N/A	445961	445980	CCACTTAGTCAATAACTACT	34	1627
1041915	N/A	N/A	446223	446242	TGCCAGCAAGCCCATGTGCT	98	1628
1041947	N/A	N/A	446796	446815	GAGCAGTACCACAGATAACC	22	1629
1041979	N/A	N/A	447542	447561	TGCTCAGTTAAAATCTGAAA	49	1630
1042011	N/A	N/A	448333	448352	CTCTAGTTTCCATAGCTTCC	42	1631
1042043	N/A	N/A	448635	448654	TTCCAAATACACCTAGAATG	68	1632
1042075	N/A	N/A	448937	448956	CTTGCCTCCCACCAGGAGAC	100	1633
1042107	N/A	N/A	449467	449486	TGATGTCATCTTCAACTGGA	27	1634
1042139	N/A	N/A	449783	449802	GGTTTTTTTCCCTTCTTTGG	8	1635
1042171	N/A	N/A	450078	450097	GATTCTTCTTTAATCACTTC	31	1636
1042203	N/A	N/A	450777	450796	CTCATCATCTTCTCAATTTC	86	1637
1042235	N/A	N/A	451509	451528	CACAAACAACAATCATGTAC	47	1638
1042267	N/A	N/A	451802	451821	CTACAAGCCCTTTATAACAG	26	1639
1042299	N/A	N/A	452101	452120	TATTCTTGCCCAACACCAGG	80	1640
1042331	N/A	N/A	452409	452428	GGTTTCAAAACTACATTTAC	58	1641
1042363	N/A	N/A	452840	452859	TCTCAGGTACAAACTTTACA	26	1642
1042395	N/A	N/A	453676	453695	TTCACCATCAACAGATCTGC	80	1643
1042427	N/A	N/A	454375	454394	AGACAGTTTCAAGAAGGCCT	111	1644
1042459	N/A	N/A	455186	455205	TCAGATCTTAAAAAAGGATG	102	1645
1042491	N/A	N/A	456123	456142	AAGATAGTAAAAAGGCCAGG	135	1646
1042523	N/A	N/A	456821	456840	ATCGAACCCCAGTAATGACA	38	1647

Table 23

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040092	1188	1207	435907	435926	TTGTGTAAACCTATTCCCTG	17	1648
1040124	2971	2990	457224	457243	ACACGGCAAATCAAAGAGCT	93	1649
1040156	3526	3545	457779	457798	AAGGTTAGAACAGAAACCTA	94	1650
1040188	4228	4247	458481	458500	CACCCCCAACCCCCCTTACC	112	1651
1040220	4721	4740	458974	458993	CCCTTTAAACCACATTGAAA	59	1652
1040252	5005	5024	459258	459277	CCCCAAACCTTTCCCACAAT	53	1653
1040284	5387	5406	459640	459659	ATGATATTTCGGATCTCTGG	11	1654
1040316	5699	5718	459952	459971	GTCAAGGAACTATTCTAGCT	22	1655
1040348	6113	6132	460366	460385	ATTCCTATACCTGAAATAGA	51	1656
1040380	6874	6893	461127	461146	CACCGAAGAATTTCTACCCC	54	1657
1040412	7385	7404	461638	461657	CTCACAATTCCAAGTTAGAA	23	1658
1040444	7827	7846	462080	462099	AGTAGTCACAGATGTTAAAG	16	1659
1040476	8211	8230	462464	462483	GATGTGTTCTTAAATTCTCT	14	1660
1040508	8526	8545	462779	462798	ACCTGTACTCCTCAAAGTGA	58	1661
1040540	8845	8864	463098	463117	AACAGTATTCTCAAATCGCA	73	1662
1040572	9267	9286	463520	463539	CTTAATATCCCCACAGCTGT	108	1663
1040604	9597	9616	463850	463869	TTGGCCATCCAGACAGCAAA	96	1664
1040636	10153	10172	464406	464425	TGCCCTCAACCCAAGTTCTG	82	1665
1040668	10376	10395	464629	464648	ATATGAATTCTTCCATTTTT	91	1666
1040700	N/A	N/A	7886	7905	CGTTATAAAATATATTACTA	97	1667
1040732	N/A	N/A	24555	24574	GCAAGATGAATTTATCCTCC	11	1668
1040764	N/A	N/A	38983	39002	CACAACTTATTTTAATGTCA	13	1669
1040796	N/A	N/A	66238	66257	TGAGTATTTTAAACTCTTCT	138	1670
1040828	N/A	N/A	83133	83152	ATTCCATTATTTTAGAAAGC	50	1671
1040860	N/A	N/A	105795	105814	ACTTGCAAAATTTCAAGTTT	131	1672
1040892	N/A	N/A	138729	138748	AGCAAGTTAATTTATGGCCA	101	1673
1040924	N/A	N/A	163155	163174	GATTGAATCATTTACCTCGC	49	1674
1040956	N/A	N/A	185759	185778	ATCTGCTTTCTTTATTCCCT	9	1675
1040988	N/A	N/A	207251	207270	ATCTCTGTTATTTAACACTG	70	1676
1041020	N/A	N/A	224368	224387	TTCTTTAAAACTATTAGTCA	122	1677
1041052	N/A	N/A	245320	245339	GACCTCAAAACCAAATTAGG	119	1678
1041084	N/A	N/A	268039	268058	TCTGAAATTCAAAATCAGTG	122	1679
1041116	N/A	N/A	284543	284562	CCACTGGAAATTTAACATGA	18	1680
1041148	N/A	N/A	315438	315457	TGTATCACCCATTAACTGAC	2	1681
1041180	N/A	N/A	332732	332751	GACTAAAAAATATACATCTC	57	1682
1041212	N/A	N/A	356967	356986	GGTCTATTTCTTTACAGCAC	2	1683
1041244	N/A	N/A	376250	376269	TTCTTCTGTATTTAATTCTT	18	1684
1041276	N/A	N/A	407619	407638	ACTGAGTTTCAAAGCAAAGA	30	1685

1041308	N/A	N/A	433762	433781	ATCCGATTTTAAAACAAACA	64	1686
1041340	N/A	N/A	438045	438064	AGACATATTTTAAAACATGG	29	1687
1041372	N/A	N/A	438476	438495	TAACCAATCCTAAACCCGTT	97	1688
1041404	N/A	N/A	439022	439041	ATTAGCTAATTCCTAGAGGC	60	1689
1041436	N/A	N/A	439388	439407	TGAATGTTTTCAAATCCTAG	31	1690
1041468	N/A	N/A	440075	440094	CCATTTATTTTAAAAATCCT	69	1691
1041500	N/A	N/A	440312	440331	CATTTCTAAACAAAACCTCT	95	1692
1041532	N/A	N/A	440910	440929	CAGTAGAGAGATTTAGTGAT	15	1693
1041564	N/A	N/A	441493	441512	TGGAGAAAACCATCTCTTCT	126	1694
1041596	N/A	N/A	442101	442120	GTGAAGCATTAAAAAACGGA	28	1695
1041628	N/A	N/A	442500	442519	CTGGCATTCCCCTTTCCTCC	92	1696
1041660	N/A	N/A	442985	443004	TTGATTTATTTTTCAGCTGT	30	1697
1041692	N/A	N/A	443241	443260	CCAATGCACCCCTCAAATCC	147	1698
1041724	N/A	N/A	443784	443803	CCGATGACTCACAGCTCACA	46	1699
1041756	N/A	N/A	444141	444160	GAGAGCATTTTTCTCCTTTT	25	1700
1041788	N/A	N/A	444741	444760	GAACAACATAATATTCAGTG	10	1701
1041820	N/A	N/A	445425	445444	TCATTAATAAAAACAGTCAA	102	1702
1041852	N/A	N/A	445718	445737	TGACACTATCCCAGACATAC	34	1703
1041884	N/A	N/A	445963	445982	CACCACTTAGTCAATAACTA	38	1704
1041916	N/A	N/A	446261	446280	CCACCCTCCTCCACTCTTTC	138	1705
1041948	N/A	N/A	446798	446817	GGGAGCAGTACCACAGATAA	34	1706
1041980	N/A	N/A	447543	447562	GTGCTCAGTTAAAATCTGAA	29	1707
1042012	N/A	N/A	448335	448354	CCCTCTAGTTTCCATAGCTT	60	1708
1042044	N/A	N/A	448638	448657	CTTTTCCAAATACACCTAGA	46	1709
1042076	N/A	N/A	448955	448974	TTGGTTAAGACCTAGTTTCT	52	1710
1042108	N/A	N/A	449502	449521	TGGATGTGAAACAGAGACGG	17	1711
1042140	N/A	N/A	449787	449806	ATAAGGTTTTTTTCCCTTCT	48	1712
1042172	N/A	N/A	450079	450098	AGATTCTTCTTTAATCACTT	39	1713
1042204	N/A	N/A	450800	450819	GAGATGGTACTTTAGAAGGC	14	1714
1042236	N/A	N/A	451510	451529	ACACAAACAACAATCATGTA	56	1715
1042268	N/A	N/A	451805	451824	TGTCTACAAGCCCTTTATAA	50	1716
1042300	N/A	N/A	452105	452124	TGCTTATTCTTGCCCAACAC	35	1717
1042332	N/A	N/A	452410	452429	TGGTTTCAAAACTACATTTA	105	1718
1042364	N/A	N/A	452899	452918	GGCTATTTTTATAATGTGAA	25	1719
1042396	N/A	N/A	453692	453711	ACAGTAATTAAAAGAATTCA	88	1720
1042428	N/A	N/A	454436	454455	CAGAAGTTAATACTTGAGGA	71	1721
1042460	N/A	N/A	455194	455213	GCAAAATATCAGATCTTAAA	65	1722
1042492	N/A	N/A	456134	456153	GGACAGCAAATAAGATAGTA	48	1723
1042524	N/A	N/A	456828	456847	CCAGTCAATCGAACCCCAGT	85	1724

Table 24

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	1	138
1040093	1189	1208	435908	435927	TTTGTGTAAACCTATTCCCT	23	1725
1040125	2998	3017	457251	457270	GCAGACATCCCCAACTGAGA	41	1726
1040157	3559	3578	457812	457831	CTCCTGCGACACACCTGCTG	58	1727
1040189	4287	4306	458540	458559	ATTGGTTTTCCTAACACTGC	54	1728
1040221	4722	4741	458975	458994	TCCCTTTAAACCACATTGAA	65	1729
1040253	5006	5025	459259	459278	CCCCCAAACCTTTCCCACAA	61	1730
1040285	5394	5413	459647	459666	CCCACAAATGATATTTCGGA	20	1731
1040317	5719	5738	459972	459991	GGTAATGAAATTCGAGGAAA	12	1732
1040349	6120	6139	460373	460392	TTTTATAATTCCTATACCTG	61	1733
1040381	6876	6895	461129	461148	GGCACCGAAGAATTTCTACC	28	1734
1040413	7386	7405	461639	461658	GCTCACAATTCCAAGTTAGA	17	1735
1040445	7830	7849	462083	462102	CTTAGTAGTCACAGATGTTA	27	1736
1040477	8225	8244	462478	462497	TATATTTATTACTTGATGTG	24	1737
1040509	8541	8560	462794	462813	ATTTTTTAAAACATTACCTG	112	1738
1040541	8869	8888	463122	463141	AGAAGTACTTTCAGCATAGG	12	1739
1040573	9268	9287	463521	463540	GCTTAATATCCCCACAGCTG	120	1740
1040605	9624	9643	463877	463896	TTGGCCACAGAAAAGGAGAC	110	1741
1040637	10159	10178	464412	464431	TGGTAGTGCCCTCAACCCAA	43	1742
1040669	10394	10413	464647	464666	CCACGATTAGAAAATAGAAT	108	1743
1040701	N/A	N/A	8020	8039	TCAAACAAAATATAATGCTT	87	1744
1040733	N/A	N/A	24636	24655	CTACACAAAACCAATCACTT	78	1745
1040765	N/A	N/A	39292	39311	CGCCTTAATTTTTATTATAG	83	1746
1040797	N/A	N/A	66579	66598	CCATTTAGAATATAGCTGTT	25	1747
1040829	N/A	N/A	83570	83589	ATTCTCATCCATTATACTTT	48	1748
1040861	N/A	N/A	106210	106229	TTACCAAAAACCATTTGTGT	21	1749
1040893	N/A	N/A	138831	138850	TCCTTCTTTCAAAGTTCACC	26	1750
1040925	N/A	N/A	163322	163341	CTGCCACTATTTTATGTCTG	59	1751
1040957	N/A	N/A	185775	185794	CCCAGGTTCCCTTATCATCT	19	1752
1040989	N/A	N/A	207430	207449	TTCTGCAAATAATTCCGTCA	23	1753
1041021	N/A	N/A	224375	224394	CCATCATTTCTTTAAAACTA	67	1754
1041053	N/A	N/A	246302	246321	AAGTACATACAAATACATAT	146	1755
1041085	N/A	N/A	268505	268524	CCTATCAAAGCCACAACTTC	117	1756
1041117	N/A	N/A	284846	284865	TTGTATACCATTTATGTTTC	2	1757
1041149	N/A	N/A	315942	315961	CCACTCAAACCTTTCAATGC	20	1758
1041181	N/A	N/A	334092	334111	GAGCTCAAACCCAAGTCTGT	72	1759
1041213	N/A	N/A	357527	357546	ACCCTATTTCCTTAATGTAA	41	1760
1041245	N/A	N/A	377993	378012	CTCCTTCACCCTTAAGGCTA	68	1761
1041277	N/A	N/A	409360	409379	ATCGAGTCCTTTTAAACAAA	19	1762

1041309	N/A	N/A	434288	434307	ACAACTCGCCATTAACACTA	65	1763
1041341	N/A	N/A	438053	438072	AGCTAATAAGACATATTTTA	109	1764
1041373	N/A	N/A	438477	438496	CTAACCAATCCTAAACCCGT	101	1765
1041405	N/A	N/A	439023	439042	GATTAGCTAATTCCTAGAGG	42	1766
1041437	N/A	N/A	439389	439408	TTGAATGTTTTCAAATCCTA	41	1767
1041469	N/A	N/A	440076	440095	GCCATTTATTTTAAAAATCC	10	1768
1041501	N/A	N/A	440313	440332	GCATTTCTAAACAAAACCTC	62	1769
1041533	N/A	N/A	441017	441036	TGAGGAAGCCCTTCCCGGCA	115	1770
1041565	N/A	N/A	441494	441513	TTGGAGAAAACCATCTCTTC	108	1771
1041597	N/A	N/A	442114	442133	GGAAAGTATAAAAGTGAAGC	25	1772
1041629	N/A	N/A	442524	442543	GCACGCAGTAACAATGGACA	31	1773
1041661	N/A	N/A	442987	443006	CTTTGATTTATTTTTCAGCT	11	1774
1041693	N/A	N/A	443288	443307	CCCTTGTTTCTGCATTGGTT	46	1775
1041725	N/A	N/A	443792	443811	TGTTACCACCGATGACTCAC	42	1776
1041757	N/A	N/A	444158	444177	GCACATACAGTTTAAAGGAG	12	1777
1041789	N/A	N/A	444885	444904	GGTCCCTGTTCCTAGGGAGG	143	1778
1041821	N/A	N/A	445439	445458	GCAATGTTTAAAAATCATTA	71	1779
1041853	N/A	N/A	445722	445741	TTCATGACACTATCCCAGAC	46	1780
1041885	N/A	N/A	445968	445987	CCTTTCACCACTTAGTCAAT	33	1781
1041917	N/A	N/A	446266	446285	GCCTCCCACCCTCCTCCACT	101	1782
1041949	N/A	N/A	446814	446833	ATGAAAATAAACTCATGGGA	84	1783
1041981	N/A	N/A	447571	447590	GTCTAAAAGACTTCCTAGCA	78	1784
1042013	N/A	N/A	448352	448371	TCTATTTAAAATAACAACCC	107	1785
1042045	N/A	N/A	448641	448660	TTCCTTTTCCAAATACACCT	59	1786
1042077	N/A	N/A	448969	448988	TAGAAGAGTATCTATTGGTT	32	1787
1042109	N/A	N/A	449541	449560	CATCTCAAAACATGCTGTCA	86	1788
1042141	N/A	N/A	449797	449816	GAGAAGTAAAATAAGGTTTT	62	1789
1042173	N/A	N/A	450080	450099	GAGATTCTTCTTTAATCACT	27	1790
1042205	N/A	N/A	451120	451139	GGAGATTTTACTTAATTTTT	8	1791
1042237	N/A	N/A	451511	451530	TACACAAACAACAATCATGT	54	1792
1042269	N/A	N/A	451817	451836	CTCATTAAGAAATGTCTACA	69	1793
1042301	N/A	N/A	452128	452147	GACTCTCTACCAGAGTTGCG	102	1794
1042333	N/A	N/A	452413	452432	ATTTGGTTTCAAAACTACAT	91	1795
1042365	N/A	N/A	452900	452919	GGGCTATTTTTATAATGTGA	20	1796
1042397	N/A	N/A	453702	453721	GTTCAGACAAACAGTAATTA	18	1797
1042429	N/A	N/A	454481	454500	ACATAATTTGAATCCTAGGA	135	1798
1042461	N/A	N/A	455196	455215	TAGCAAAATATCAGATCTTA	41	1799
1042493	N/A	N/A	456136	456155	CTGGACAGCAAATAAGATAG	35	1800
1042525	N/A	N/A	456836	456855	TGTTAGAACCAGTCAATCGA	116	1801

Table 25

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040094	1212	1231	435931	435950	TAGTCCAGCCCTGTGGACAA	47	1802
1040126	2999	3018	457252	457271	TGCAGACATCCCCAACTGAG	57	1803
1040158	3572	3591	457825	457844	CATATGCACCAGTCTCCTGC	65	1804
1040190	4299	4318	458552	458571	TGCAATAACCTGATTGGTTT	39	1805
1040222	4725	4744	458978	458997	TCATCCCTTTAAACCACATT	35	1806
1040254	5007	5026	459260	459279	TCCCCCAAACCTTTCCCACA	94	1807
1040286	5401	5420	459654	459673	TTCAAAACCCACAAATGATA	88	1808
1040318	5721	5740	459974	459993	AGGGTAATGAAATTCGAGGA	10	1809
1040350	6122	6141	460375	460394	TATTTTATAATTCCTATACC	108	1810
1040382	6919	6938	461172	461191	GGACATAGTACAGAGGCACA	8	1811
1040414	7387	7406	461640	461659	GGCTCACAATTCCAAGTTAG	32	1812
1040446	7840	7859	462093	462112	AATAGGTTTCCTTAGTAGTC	22	1813
1040478	8227	8246	462480	462499	TGTATATTTATTACTTGATG	10	1814
1040510	8546	8565	462799	462818	GTGCAATTTTTTAAAACATT	18	1815
1040542	8907	8926	463160	463179	GCAATGGCTTAAGAGTTTAG	9	1816
1040574	9269	9288	463522	463541	TGCTTAATATCCCCACAGCT	91	1817
1040606	9636	9655	463889	463908	AAGGCCTTCAGATTGGCCAC	125	1818
1040638	10161	10180	464414	464433	TCTGGTAGTGCCCTCAACCC	45	1819
1040670	10402	10421	464655	464674	TAGACACACCACGATTAGAA	68	1820
1040702	N/A	N/A	8570	8589	ACTCAATATTTTTAAAACCC	28	1821
1040734	N/A	N/A	25367	25386	GACTGAATTATTTATAGTTG	42	1822
1040766	N/A	N/A	40104	40123	ATGCAATTTTAAATTCATGT	18	1823
1040798	N/A	N/A	66787	66806	GGGAAAATTCCTTAGCATAT	30	1824
1040830	N/A	N/A	83587	83606	GCTGAGTTCCAAAGCAAATT	35	1825
1040862	N/A	N/A	106215	106234	ATGACTTACCAAAAACCATT	105	1826
1040894	N/A	N/A	139215	139234	AGGGCTTAAATTTAACTGAA	28	1827
1040926	N/A	N/A	163369	163388	AACGAAATTCCTTAAGGACA	62	1828
1040958	N/A	N/A	185909	185928	TTGGTTCTATTTTATAATAG	66	1829
1040990	N/A	N/A	207479	207498	AGACTACTATTTTATCACTG	19	1830
1041022	N/A	N/A	225966	225985	TCACTTAAACCCAGGTCAGC	81	1831
1041054	N/A	N/A	247054	247073	TTCCCCAAAATTTAGTTGTG	85	1832
1041086	N/A	N/A	268668	268687	CTTCAACTATTTTATTTGGC	30	1833
1041118	N/A	N/A	284950	284969	AGTAGAATTTAAAAGTAGAA	110	1834
1041150	N/A	N/A	316219	316238	GGATTTCTAATTTAATCTTT	37	1835
1041182	N/A	N/A	334729	334748	TAGTTCTTTCAAACTCCTTT	2	1836
1041214	N/A	N/A	358497	358516	GCTATAATTCAAAATGCTCT	115	1837
1041246	N/A	N/A	380363	380382	GCCTAAACAATTTATTCATT	31	1838
1041278	N/A	N/A	409434	409453	ACCCTTCTATTTTATAAAGC	69	1839

1041310	N/A	N/A	434517	434536	TGCAAGTTTCAAAAGAATTC	133	1840
1041342	N/A	N/A	438074	438093	AAGGCATATACCACTGTACC	61	1841
1041374	N/A	N/A	438478	438497	TCTAACCAATCCTAAACCCG	107	1842
1041406	N/A	N/A	439043	439062	AGAGGTATAGTCTCTCCTAG	29	1843
1041438	N/A	N/A	439430	439449	TGACTATTTTCAACTCAAGC	16	1844
1041470	N/A	N/A	440085	440104	TATTATTATGCCATTTATTT	41	1845
1041502	N/A	N/A	440315	440334	TCGCATTTCTAAACAAAACC	52	1846
1041534	N/A	N/A	441019	441038	TTTGAGGAAGCCCTTCCCGG	119	1847
1041566	N/A	N/A	441497	441516	GTTTTGGAGAAAACCATCTC	69	1848
1041598	N/A	N/A	442146	442165	CTAATAAATTTTTACAAGGG	72	1849
1041630	N/A	N/A	442542	442561	AAGGAGGCTTCCTTTGGTGC	70	1850
1041662	N/A	N/A	442991	443010	AGGCCTTTGATTTATTTTTC	110	1851
1041694	N/A	N/A	443385	443404	GATGGAAGCCAAAGGCTCCC	115	1852
1041726	N/A	N/A	443794	443813	AATGTTACCACCGATGACTC	71	1853
1041758	N/A	N/A	444206	444225	TCTGAGAGAATCAAAACATA	29	1854
1041790	N/A	N/A	445090	445109	CTCACTTGCCTTCCTTTTCT	46	1855
1041822	N/A	N/A	445440	445459	TGCAATGTTTAAAAATCATT	94	1856
1041854	N/A	N/A	445730	445749	AACATTTTTTCATGACACTA	10	1857
1041886	N/A	N/A	445969	445988	TCCTTTCACCACTTAGTCAA	47	1858
1041918	N/A	N/A	446324	446343	TCTGTCTTTCATCTCTGGAT	44	1859
1041950	N/A	N/A	446817	446836	CCAATGAAAATAAACTCATG	98	1860
1041982	N/A	N/A	447576	447595	CCAGAGTCTAAAAGACTTCC	110	1861
1042014	N/A	N/A	448353	448372	TTCTATTTAAAATAACAACC	116	1862
1042046	N/A	N/A	448648	448667	GTATGGGTTCCTTTTCCAAA	7	1863
1042078	N/A	N/A	449026	449045	AGTTTTAATAAAAGTTCAAC	96	1864
1042110	N/A	N/A	449542	449561	CCATCTCAAAACATGCTGTC	78	1865
1042142	N/A	N/A	449830	449849	ATGTACTTTTTCCCCCTTGG	65	1866
1042174	N/A	N/A	450083	450102	TGGGAGATTCTTCTTTAATC	19	1867
1042206	N/A	N/A	451121	451140	TGGAGATTTTACTTAATTTT	33	1868
1042238	N/A	N/A	451518	451537	GATAATATACACAAACAACA	86	1869
1042270	N/A	N/A	451821	451840	TAGACTCATTAAGAAATGTC	91	1870
1042302	N/A	N/A	452129	452148	AGACTCTCTACCAGAGTTGC	100	1871
1042334	N/A	N/A	452424	452443	TGTGTGACACTATTTGGTTT	74	1872
1042366	N/A	N/A	452902	452921	CTGGGCTATTTTTATAATGT	30	1873
1042398	N/A	N/A	453708	453727	AGACATGTTCAGACAAACAG	58	1874
1042430	N/A	N/A	454483	454502	ACACATAATTTGAATCCTAG	110	1875
1042462	N/A	N/A	455198	455217	ACTAGCAAAATATCAGATCT	49	1876
1042494	N/A	N/A	456154	456173	ACTTTTTTTCTTATAGTACT	68	1877
1042526	N/A	N/A	456838	456857	TCTGTTAGAACCAGTCAATC	51	1878

Table 26

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040095	1514	1533	436233	436252	TCAGACTGCCCATGTTGGCC	71	1879
1040127	3033	3052	457286	457305	GAGCCGTTCTTCAGGTTCTT	93	1880
1040159	3643	3662	457896	457915	GCCTGGAGCCCTGACCGCTC	60	1881
1040191	4300	4319	458553	458572	ATGCAATAACCTGATTGGTT	16	1882
1040223	4727	4746	458980	458999	ATTCATCCCTTTAAACCACA	15	1883
1040255	5011	5030	459264	459283	TCAGTCCCCCAAACCTTTCC	20	1884
1040287	5407	5426	459660	459679	GATGCATTCAAAACCCACAA	21	1885
1040319	5766	5785	460019	460038	TGACTGCAAGAATGAGCCCA	60	1886
1040351	6126	6145	460379	460398	CAATTATTTTATAATTCCTA	82	1887
1040383	6921	6940	461174	461193	GTGGACATAGTACAGAGGCA	7	1888
1040415	7388	7407	461641	461660	AGGCTCACAATTCCAAGTTA	26	1889
1040447	7865	7884	462118	462137	TGGAGATTTTTCTCTCTATG	36	1890
1040479	8228	8247	462481	462500	CTGTATATTTATTACTTGAT	7	1891
1040511	8566	8585	462819	462838	TCGACATTCATTTTTCTTTT	10	1892
1040543	8940	8959	463193	463212	ATGTCAAACATCATCTCTGA	12	1893
1040575	9272	9291	463525	463544	GGGTGCTTAATATCCCCACA	115	1894
1040607	9637	9656	463890	463909	GAAGGCCTTCAGATTGGCCA	101	1895
1040639	10163	10182	464416	464435	AGTCTGGTAGTGCCCTCAAC	17	1896
1040671	10407	10426	464660	464679	ACAAATAGACACACCACGAT	77	1897
1040703	N/A	N/A	9147	9166	GTTGAGTTACAAATATAAAT	70	1898
1040735	N/A	N/A	25394	25413	CCAGGATTTTAAAAAAAGCA	15	1899
1040767	N/A	N/A	40413	40432	GCTAAATTTCCTTAAGCTTT	42	1900
1040799	N/A	N/A	70441	70460	CATCAGTTCCAAAACCTGGA	83	1901
1040831	N/A	N/A	83929	83948	CCAATACACCTTTATTTTTC	22	1902
1040863	N/A	N/A	106559	106578	CGATTAATCCCTTATGTTTT	4	1903
1040895	N/A	N/A	140193	140212	CTCTTCAAAAACATATCCGA	55	1904
1040927	N/A	N/A	163438	163457	TTCTAAATTTAAAACTCCAA	101	1905
1040959	N/A	N/A	186773	186792	ACAGGCAATATTTACTATAA	1	1906
1040991	N/A	N/A	207544	207563	GCCTTCTTCCTTTATAGCAC	32	1907
1041023	N/A	N/A	227246	227265	TTAGGCTATTAAATAATAGA	124	1908
1041055	N/A	N/A	247203	247222	CTCAGTATCTTTTAATTGCC	29	1909
1041087	N/A	N/A	269929	269948	TGGGCCAAAAACACCCCTTT	95	1910
1041119	N/A	N/A	284975	284994	CTGTTTAAAAATGTATTGAG	23	1911
1041151	N/A	N/A	316940	316959	GTCCCTTATCCTTAACACAC	2	1912
1041183	N/A	N/A	334783	334802	CCCTAAATTTAAATTCTCTG	62	1913
1041215	N/A	N/A	358611	358630	ACCTTTATTTAAATTTTCCA	22	1914
1041247	N/A	N/A	380517	380536	GCTCAATATATTTATCTATT	1	1915
1041279	N/A	N/A	410051	410070	TCTGTATTTTAAAAATCTCT	27	1916

1041311	N/A	N/A	437693	437712	CGAGAACCCTTAATCCTGCC	34	1917
1041343	N/A	N/A	438076	438095	CGAAGGCATATACCACTGTA	48	1918
1041375	N/A	N/A	438482	438501	CCACTCTAACCAATCCTAAA	48	1919
1041407	N/A	N/A	439087	439106	TTTTATTTTCTGATGCTTTG	10	1920
1041439	N/A	N/A	439432	439451	CATGACTATTTTCAACTCAA	4	1921
1041471	N/A	N/A	440089	440108	GCTGTATTATTATGCCATTT	12	1922
1041503	N/A	N/A	440316	440335	GTCGCATTTCTAAACAAAAC	64	1923
1041535	N/A	N/A	441116	441135	AGTGACAAATCATTGGTTGC	28	1924
1041567	N/A	N/A	441513	441532	AGTCACAATGCCATCTGTTT	10	1925
1041599	N/A	N/A	442147	442166	GCTAATAAATTTTTACAAGG	56	1926
1041631	N/A	N/A	442566	442585	TGCTATCACCCTCCACTGAA	85	1927
1041663	N/A	N/A	443017	443036	CTTCCATAAACTCTTTTTAG	45	1928
1041695	N/A	N/A	443387	443406	CAGATGGAAGCCAAAGGCTC	117	1929
1041727	N/A	N/A	443815	443834	CAGCTAATCCATTCAATGCA	60	1930
1041759	N/A	N/A	444223	444242	GCTATAAACAACAACAGTCT	26	1931
1041791	N/A	N/A	445120	445139	CACGGAAGCCCTTAGGCACA	63	1932
1041823	N/A	N/A	445455	445474	GAGAGACCCATTTACTGCAA	8	1933
1041855	N/A	N/A	445739	445758	GTTTTACAAAACATTTTTTC	56	1934
1041887	N/A	N/A	445972	445991	AATTCCTTTCACCACTTAGT	16	1935
1041919	N/A	N/A	446325	446344	CTCTGTCTTTCATCTCTGGA	49	1936
1041951	N/A	N/A	446818	446837	CCCAATGAAAATAAACTCAT	77	1937
1041983	N/A	N/A	447604	447623	CTCTTTCCCCAAACTCAGTG	30	1938
1042015	N/A	N/A	448354	448373	GTTCTATTTAAAATAACAAC	109	1939
1042047	N/A	N/A	448660	448679	TATAAGCAAACTGTATGGGT	13	1940
1042079	N/A	N/A	449037	449056	TCAGGCTTTCCAGTTTTAAT	16	1941
1042111	N/A	N/A	449544	449563	CTCCATCTCAAAACATGCTG	82	1942
1042143	N/A	N/A	449832	449851	CAATGTACTTTTTCCCCCTT	32	1943
1042175	N/A	N/A	450112	450131	AATGAAATTTATGTTAACCT	75	1944
1042207	N/A	N/A	451122	451141	TTGGAGATTTTACTTAATTT	30	1945
1042239	N/A	N/A	451523	451542	ACCGAGATAATATACACAAA	5	1946
1042271	N/A	N/A	451863	451882	TAGGTAAACTTATCTGAGGA	15	1947
1042303	N/A	N/A	452153	452172	TCAGGTGTTAACATCTGTCT	99	1948
1042335	N/A	N/A	452453	452472	CTCATACAATTCTAGTTACC	45	1949
1042367	N/A	N/A	452919	452938	GGGAAAGTTTCATTGTTCTG	24	1950
1042399	N/A	N/A	453742	453761	GCAAAAAGATCCTTCCAGAA	62	1951
1042431	N/A	N/A	454491	454510	GCTAACAGACACATAATTTG	111	1952
1042463	N/A	N/A	455199	455218	CACTAGCAAAATATCAGATC	54	1953
1042495	N/A	N/A	456155	456174	AACTTTTTTTCTTATAGTAC	66	1954
1042527	N/A	N/A	456877	456896	TTCAAAATATTCCATCAAGT	25	1955

Table 27

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	1	138
1040096	1932	1951	436651	436670	TCACCGTTCAGGACCTCCTT	70	1956
1040128	3046	3065	457299	457318	GCCCTTTTTAACAGAGCCGT	122	1957
1040160	3669	3688	457922	457941	GCCCCGTTCCTTTCTTCCCC	67	1958
1040192	4313	4332	458566	458585	GGGAGTGAAGTCAATGCAAT	17	1959
1040224	4728	4747	458981	459000	CATTCATCCCTTTAAACCAC	22	1960
1040256	5013	5032	459266	459285	GTTCAGTCCCCCAAACCTTT	16	1961
1040288	5408	5427	459661	459680	AGATGCATTCAAAACCCACA	21	1962
1040320	5785	5804	460038	460057	CAGCACTAAATAAGCAGTAT	11	1963
1040352	6128	6147	460381	460400	ACCAATTATTTTATAATTCC	59	1964
1040384	6941	6960	461194	461213	CTGTCGGTAAATATTGCAAA	10	1965
1040416	7404	7423	461657	461676	CTAACAGAAAACATAGAGGC	28	1966
1040448	7866	7885	462119	462138	TTGGAGATTTTTCTCTCTAT	54	1967
1040480	8229	8248	462482	462501	TCTGTATATTTATTACTTGA	10	1968
1040512	8597	8616	462850	462869	GCCATATCTTTCAAACACTG	8	1969
1040544	8941	8960	463194	463213	AATGTCAAACATCATCTCTG	13	1970
1040576	9292	9311	463545	463564	AATTTAAGAATTGTAAGTGG	123	1971
1040608	9640	9659	463893	463912	AACGAAGGCCTTCAGATTGG	107	1972
1040640	10189	10208	464442	464461	TAGTTCTCCTCTGTACTGGC	14	1973
1040672	10409	10428	464662	464681	CTACAAATAGACACACCACG	70	1974
1040704	N/A	N/A	9365	9384	AACAGTAGCCAAAATGTTCT	100	1975
1040736	N/A	N/A	25410	25429	CTAGAATTTTAAAAAACCAG	80	1976
1040768	N/A	N/A	40502	40521	AGTACAATCTTTTATAGATA	89	1977
1040800	N/A	N/A	70463	70482	TGCCTGAGAATTTAATACTA	72	1978
1040832	N/A	N/A	84147	84166	AGTAAGCTTCTTTAACTTTA	11	1979
1040864	N/A	N/A	107690	107709	TGGATAATTATTTAATTCAT	70	1980
1040896	N/A	N/A	140329	140348	CCAAACTAAGAATAATCTAG	89	1981
1040928	N/A	N/A	165500	165519	GAGGAAATTATTTACTGGCT	5	1982
1040960	N/A	N/A	187228	187247	ATGCACATACAAATAAGCTC	51	1983
1040992	N/A	N/A	207564	207583	GAGATTAAAATACAATTGCT	36	1984
1041024	N/A	N/A	227353	227372	GATTTCTCCTTTTAACCTCT	23	1985
1041056	N/A	N/A	248796	248815	TTCTCAAAACCTTATCTCCT	92	1986
1041088	N/A	N/A	270452	270471	CATTTTATTCCTTATCCTAC	118	1987
1041120	N/A	N/A	285644	285663	CATTTGCACCTTTAATTTGT	24	1988
1041152	N/A	N/A	316955	316974	TTCCAAAAAGAATGTGTCCC	16	1989
1041184	N/A	N/A	335393	335412	GGTAGCTATCATTATTAAGC	19	1990
1041216	N/A	N/A	358821	358840	CGACAGAAAATATATCTGCT	47	1991
1041248	N/A	N/A	382312	382331	GACTGCAAAATTCCCATTGC	28	1992
1041280	N/A	N/A	410115	410134	CTGTAAAAATACACATCCTC	38	1993

1041312	N/A	N/A	437695	437714	CCCGAGAACCCTTAATCCTG	37	1994
1041344	N/A	N/A	438160	438179	CACAGGTTCAGCCATAGCTC	21	1995
1041376	N/A	N/A	438483	438502	TCCACTCTAACCAATCCTAA	66	1996
1041408	N/A	N/A	439090	439109	CGCTTTTATTTTCTGATGCT	20	1997
1041440	N/A	N/A	439433	439452	TCATGACTATTTTCAACTCA	18	1998
1041472	N/A	N/A	440090	440109	AGCTGTATTATTATGCCATT	43	1999
1041504	N/A	N/A	440317	440336	AGTCGCATTTCTAAACAAAA	66	2000
1041536	N/A	N/A	441117	441136	AAGTGACAAATCATTGGTTG	21	2001
1041568	N/A	N/A	441519	441538	GCCTAGAGTCACAATGCCAT	33	2002
1041600	N/A	N/A	442148	442167	CGCTAATAAATTTTTACAAG	91	2003
1041632	N/A	N/A	442620	442639	TCAACCAGAATCAAGGCATG	66	2004
1041664	N/A	N/A	443022	443041	CTCTCCTTCCATAAACTCTT	69	2005
1041696	N/A	N/A	443410	443429	GATGGGATAATATAGAACGC	45	2006
1041728	N/A	N/A	443816	443835	CCAGCTAATCCATTCAATGC	34	2007
1041760	N/A	N/A	444225	444244	ATGCTATAAACAACAACAGT	47	2008
1041792	N/A	N/A	445122	445141	GACACGGAAGCCCTTAGGCA	46	2009
1041824	N/A	N/A	445457	445476	GCGAGAGACCCATTTACTGC	11	2010
1041856	N/A	N/A	445746	445765	GGCATCTGTTTTACAAAACA	9	2011
1041888	N/A	N/A	445977	445996	AATAAAATTCCTTTCACCAC	35	2012
1041920	N/A	N/A	446352	446371	CTTTATACTTTTGTAAGCTT	29	2013
1041952	N/A	N/A	446819	446838	TCCCAATGAAAATAAACTCA	108	2014
1041984	N/A	N/A	447606	447625	GCCTCTTTCCCCAAACTCAG	29	2015
1042016	N/A	N/A	448356	448375	CAGTTCTATTTAAAATAACA	117	2016
1042048	N/A	N/A	448668	448687	ATCCCAATTATAAGCAAACT	64	2017
1042080	N/A	N/A	449039	449058	TTTCAGGCTTTCCAGTTTTA	20	2018
1042112	N/A	N/A	449545	449564	TCTCCATCTCAAAACATGCT	108	2019
1042144	N/A	N/A	449841	449860	CTACCTAGACAATGTACTTT	86	2020
1042176	N/A	N/A	450127	450146	CCCACCTGGCCTGTTAATGA	86	2021
1042208	N/A	N/A	451135	451154	CCAGCCTAAAAAATTGGAGA	94	2022
1042240	N/A	N/A	451524	451543	CACCGAGATAATATACACAA	18	2023
1042272	N/A	N/A	451875	451894	ACTGTGTTCTCATAGGTAAA	32	2024
1042304	N/A	N/A	452173	452192	AAGTCATAAAAATAAAACTC	99	2025
1042336	N/A	N/A	452454	452473	ACTCATACAATTCTAGTTAC	44	2026
1042368	N/A	N/A	452952	452971	AGCATGAACCCCTTCTCCTG	78	2027
1042400	N/A	N/A	453743	453762	AGCAAAAAGATCCTTCCAGA	90	2028
1042432	N/A	N/A	454556	454575	ATAGAGACAAAAAGATGGTC	104	2029
1042464	N/A	N/A	455200	455219	GCACTAGCAAAATATCAGAT	28	2030
1042496	N/A	N/A	456172	456191	TCTGGACAAAATGTTTAAAC	35	2031
1042528	N/A	N/A	456881	456900	AATATTCAAAATATTCCATC	64	2032

Table 28

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040097	1933	1952	436652	436671	CTCACCGTTCAGGACCTCCT	73	2033
1040129	3048	3067	457301	457320	TGGCCCTTTTTAACAGAGCC	113	2034
1040161	3670	3689	457923	457942	AGCCCCGTTCCTTTCTTCCC	46	2035
1040193	4328	4347	458581	458600	TTGCATCTACCTCTTGGGAG	44	2036
1040225	4729	4748	458982	459001	ACATTCATCCCTTTAAACCA	33	2037
1040257	5032	5051	459285	459304	GCTACATTTATTTATGCTCG	14	2038
1040289	5417	5436	459670	459689	GCACTTTAAAGATGCATTCA	29	2039
1040321	5786	5805	460039	460058	ACAGCACTAAATAAGCAGTA	28	2040
1040353	6129	6148	460382	460401	AACCAATTATTTTATAATTC	112	2041
1040385	6942	6961	461195	461214	GCTGTCGGTAAATATTGCAA	36	2042
1040417	7406	7425	461659	461678	ACCTAACAGAAAACATAGAG	36	2043
1040449	7882	7901	462135	462154	AGTGTCTTCAAAAGCATTGG	22	2044
1040481	8231	8250	462484	462503	TCTCTGTATATTTATTACTT	10	2045
1040513	8598	8617	462851	462870	AGCCATATCTTTCAAACACT	8	2046
1040545	8973	8992	463226	463245	TCTTTGGGTTTATAGGAACA	14	2047
1040577	9297	9316	463550	463569	TTCTGAATTTAAGAATTGTA	83	2048
1040609	9647	9666	463900	463919	CACTTCCAACGAAGGCCTTC	100	2049
1040641	10192	10211	464445	464464	CCCTAGTTCTCCTCTGTACT	79	2050
1040673	10414	10433	464667	464686	GTATCCTACAAATAGACACA	56	2051
1040705	N/A	N/A	9443	9462	ACTCACTATTTTTAAGAGCA	49	2052
1040737	N/A	N/A	25793	25812	CTGGGAATTTAAAAAACAAA	77	2053
1040769	N/A	N/A	40905	40924	TCCATAAACATTTATACAGA	5	2054
1040801	N/A	N/A	71139	71158	GGTTCAAAACCTTAGTCAGA	69	2055
1040833	N/A	N/A	85391	85410	ATAGAATATTTTTATCATTC	91	2056
1040865	N/A	N/A	108193	108212	GAATAAATTATTTACTGCGG	8	2057
1040897	N/A	N/A	140551	140570	GGTCAATTTCAAACTGTTCT	5	2058
1040929	N/A	N/A	166245	166264	GGCCTAAAACTATTCTTGAT	118	2059
1040961	N/A	N/A	187483	187502	ACACTTAAACCTGTTAATAT	78	2060
1040993	N/A	N/A	208043	208062	GCTCATAAAATACCTCTCTA	16	2061
1041025	N/A	N/A	227432	227451	CCAGGAAAGATTTATTTAGC	51	2062
1041057	N/A	N/A	250936	250955	AGCACATTTCAAAAGTTCAG	53	2063
1041089	N/A	N/A	270476	270495	ATTCATTTTCCTTATGTTAC	58	2064
1041121	N/A	N/A	286774	286793	TCACCCAAACCCATTGCCTA	77	2065
1041153	N/A	N/A	317256	317275	TTCTGTAAAATATATCCTGT	19	2066
1041185	N/A	N/A	335931	335950	ATCTGTAAAATATGGTTGCA	7	2067
1041217	N/A	N/A	362937	362956	AACTTATTTTAAAGTGTCCA	2	2068
1041249	N/A	N/A	385646	385665	ACATTATACCCTTAATATCC	39	2069
1041281	N/A	N/A	410116	410135	GCTGTAAAAATACACATCCT	18	2070

1041313	N/A	N/A	437751	437770	GCTTATTTTTTCTAGAGAAC	54	2071
1041345	N/A	N/A	438169	438188	AGTGATAGTCACAGGTTCAG	12	2072
1041377	N/A	N/A	438486	438505	TTATCCACTCTAACCAATCC	101	2073
1041409	N/A	N/A	439093	439112	CCACGCTTTTATTTTCTGAT	1	2074
1041441	N/A	N/A	439441	439460	CAGCTATTTCATGACTATTT	7	2075
1041473	N/A	N/A	440091	440110	GAGCTGTATTATTATGCCAT	107	2076
1041505	N/A	N/A	440318	440337	CAGTCGCATTTCTAAACAAA	76	2077
1041537	N/A	N/A	441122	441141	CGGTAAAGTGACAAATCATT	12	2078
1041569	N/A	N/A	441521	441540	CTGCCTAGAGTCACAATGCC	31	2079
1041601	N/A	N/A	442149	442168	ACGCTAATAAATTTTTACAA	109	2080
1041633	N/A	N/A	442624	442643	ACTCTCAACCAGAATCAAGG	86	2081
1041665	N/A	N/A	443023	443042	CCTCTCCTTCCATAAACTCT	85	2082
1041697	N/A	N/A	443457	443476	CTGTGTACTCTTCAGAGAAG	27	2083
1041729	N/A	N/A	443817	443836	ACCAGCTAATCCATTCAATG	17	2084
1041761	N/A	N/A	444251	444270	AACAATAGTCTTTAATTTTT	109	2085
1041793	N/A	N/A	445143	445162	GTGAGTGACCACAGCAGCTG	110	2086
1041825	N/A	N/A	445458	445477	AGCGAGAGACCCATTTACTG	23	2087
1041857	N/A	N/A	445767	445786	CTGTTTTCACAAATTGCGAA	44	2088
1041889	N/A	N/A	445978	445997	CAATAAAATTCCTTTCACCA	37	2089
1041921	N/A	N/A	446354	446373	GCCTTTATACTTTTGTAAGC	73	2090
1041953	N/A	N/A	446832	446851	GTTTCTGATTAAATCCCAAT	18	2091
1041985	N/A	N/A	447607	447626	TGCCTCTTTCCCCAAACTCA	47	2092
1042017	N/A	N/A	448370	448389	GAGAACTCCCCTGACAGTTC	90	2093
1042049	N/A	N/A	448679	448698	ACATCACAAACATCCCAATT	71	2094
1042081	N/A	N/A	449045	449064	GATACATTTCAGGCTTTCCA	13	2095
1042113	N/A	N/A	449571	449590	CTTGAAATTCCCTTGGAGAG	42	2096
1042145	N/A	N/A	449843	449862	AACTACCTAGACAATGTACT	65	2097
1042177	N/A	N/A	450452	450471	CGTACTAAAACAAGATGACG	51	2098
1042209	N/A	N/A	451136	451155	ACCAGCCTAAAAAATTGGAG	72	2099
1042241	N/A	N/A	451525	451544	GCACCGAGATAATATACACA	13	2100
1042273	N/A	N/A	451891	451910	TCTGAAAATAACATCTACTG	43	2101
1042305	N/A	N/A	452175	452194	CCAAGTCATAAAAATAAAAC	104	2102
1042337	N/A	N/A	452460	452479	ATAGCCACTCATACAATTCT	34	2103
1042369	N/A	N/A	452953	452972	AAGCATGAACCCCTTCTCCT	66	2104
1042401	N/A	N/A	453745	453764	GGAGCAAAAAGATCCTTCCA	91	2105
1042433	N/A	N/A	454600	454619	GGATTCTCTAATTAGAGCTT	41	2106
1042465	N/A	N/A	455224	455243	GAGGAGACCAGATAGCTTGT	79	2107
1042497	N/A	N/A	456173	456192	CTCTGGACAAAATGTTTAAA	82	2108
1042529	N/A	N/A	456883	456902	TCAATATTCAAAATATTCCA	98	2109

Table 29

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040098	2110	2129	436829	436848	GGGCAGGACCATCACAGAGG	60	2110
1040130	3049	3068	457302	457321	CTGGCCCTTTTTAACAGAGC	107	2111
1040162	3765	3784	458018	458037	CTGCAGGACCCTTCCCACGG	118	2112
1040194	4393	4412	458646	458665	TCAAAGACAAAAAGATTTCG	75	2113
1040226	4733	4752	458986	459005	ATTCACATTCATCCCTTTAA	35	2114
1040258	5048	5067	459301	459320	GTTAGAAAGAAATTTTGCTA	58	2115
1040290	5442	5461	459695	459714	CCTACTTATAAAACTTTTTT	114	2116
1040322	5787	5806	460040	460059	TACAGCACTAAATAAGCAGT	68	2117
1040354	6177	6196	460430	460449	CACATGCTAAAAAAGCAAGA	86	2118
1040386	6960	6979	461213	461232	AAGAAAGAACAAAAGACGGC	66	2119
1040418	7407	7426	461660	461679	CACCTAACAGAAAACATAGA	118	2120
1040450	7883	7902	462136	462155	TAGTGTCTTCAAAAGCATTG	39	2121
1040482	8238	8257	462491	462510	AGTATATTCTCTGTATATTT	29	2122
1040514	8599	8618	462852	462871	GAGCCATATCTTTCAAACAC	25	2123
1040546	8986	9005	463239	463258	TTCAAGATTATATTCTTTGG	52	2124
1040578	9328	9347	463581	463600	GTTGCCTTCAACGAGAAGGG	62	2125
1040610	9658	9677	463911	463930	ACTGTAAACAACACTTCCAA	22	2126
1040642	10204	10223	464457	464476	ACATCATTCCTTCCCTAGTT	29	2127
1040674	10415	10434	464668	464687	TGTATCCTACAAATAGACAC	78	2128
1040706	N/A	N/A	9658	9677	GGCTGATTTTAAACTTAGTT	31	2129
1040738	N/A	N/A	26160	26179	GTTTTATATTTTTAAGTGCT	7	2130
1040770	N/A	N/A	40931	40950	ACATTTAAAATATTTCAGAC	108	2131
1040802	N/A	N/A	71486	71505	TGTCTATTTTAAAGACTCAA	112	2132
1040834	N/A	N/A	85731	85750	GGATATCTATTTTAATTCTT	62	2133
1040866	N/A	N/A	108791	108810	ACAGTATTTCAAAAGAAGCC	73	2134
1040898	N/A	N/A	140712	140731	CTGGATAATACCTAACTGTC	58	2135
1040930	N/A	N/A	167395	167414	AGTGACTTAGATTATCCTTT	17	2136
1040962	N/A	N/A	187991	188010	CACATCAAACCTCAAGGGCA	64	2137
1040994	N/A	N/A	208238	208257	GTTTCCCTAATTTATGGAGT	52	2138
1041026	N/A	N/A	227529	227548	ATTCTTACAATTTACTTGTA	96	2139
1041058	N/A	N/A	251431	251450	ATTCTCTTTTAAAGATAAAG	119	2140
1041090	N/A	N/A	270489	270508	CTATGGTTTTAAAATTCATT	82	2141
1041122	N/A	N/A	287171	287190	ACTACCAGCCCTTATTTCAG	20	2142
1041154	N/A	N/A	318500	318519	CTCTGCTTTCAAATGTGTTT	6	2143
1041186	N/A	N/A	338862	338881	TCTTTCATATTTTAAAGTGC	3	2144
1041218	N/A	N/A	365191	365210	TCCAGTAAAAACACAACACT	44	2145
1041250	N/A	N/A	385654	385673	TATAATATACATTATACCCT	78	2146
1041282	N/A	N/A	410286	410305	CCACAATTACAAACACACTT	41	2147

1041314	N/A	N/A	437752	437771	GGCTTATTTTTTCTAGAGAA	18	2148
1041346	N/A	N/A	438171	438190	GCAGTGATAGTCACAGGTTC	19	2149
1041378	N/A	N/A	438490	438509	GGAATTATCCACTCTAACCA	56	2150
1041410	N/A	N/A	439101	439120	TGTATTAACCACGCTTTTAT	31	2151
1041442	N/A	N/A	439443	439462	AGCAGCTATTTCATGACTAT	19	2152
1041474	N/A	N/A	440093	440112	GTGAGCTGTATTATTATGCC	62	2153
1041506	N/A	N/A	440327	440346	GCAAGGAACCAGTCGCATTT	56	2154
1041538	N/A	N/A	441144	441163	AGCCGATTTCTGATAGGCTC	78	2155
1041570	N/A	N/A	441530	441549	GCAGGATTTCTGCCTAGAGT	39	2156
1041602	N/A	N/A	442188	442207	ATGTTCATCTTAATGCTCTT	21	2157
1041634	N/A	N/A	442625	442644	GACTCTCAACCAGAATCAAG	111	2158
1041666	N/A	N/A	443025	443044	TGCCTCTCCTTCCATAAACT	89	2159
1041698	N/A	N/A	443481	443500	TTTTACAACTCCACTGAGCA	53	2160
1041730	N/A	N/A	443834	443853	CTCGGCTATTTTTAGGTACC	51	2161
1041762	N/A	N/A	444258	444277	TGCTTTAAACAATAGTCTTT	81	2162
1041794	N/A	N/A	445146	445165	CCAGTGAGTGACCACAGCAG	99	2163
1041826	N/A	N/A	445484	445503	ACCCCGTCTCAAAGATGAAG	102	2164
1041858	N/A	N/A	445769	445788	CCCTGTTTTCACAAATTGCG	62	2165
1041890	N/A	N/A	445979	445998	TCAATAAAATTCCTTTCACC	60	2166
1041922	N/A	N/A	446355	446374	GGCCTTTATACTTTTGTAAG	103	2167
1041954	N/A	N/A	446834	446853	TGGTTTCTGATTAAATCCCA	49	2168
1041986	N/A	N/A	447630	447649	TTTACTTGTATATTTGTCTG	15	2169
1042018	N/A	N/A	448384	448403	CTGTCCTTTTCAGAGAGAAC	88	2170
1042050	N/A	N/A	448680	448699	TACATCACAAACATCCCAAT	97	2171
1042082	N/A	N/A	449048	449067	AATGATACATTTCAGGCTTT	47	2172
1042114	N/A	N/A	449591	449610	ATATATCATCAAATCTGTTG	44	2173
1042146	N/A	N/A	449851	449870	TTAGTGTGAACTACCTAGAC	85	2174
1042178	N/A	N/A	450505	450524	CTGCCGAAAAATTCACGAGA	95	2175
1042210	N/A	N/A	451137	451156	AACCAGCCTAAAAAATTGGA	88	2176
1042242	N/A	N/A	451539	451558	AGGATAATTTTATGGCACCG	14	2177
1042274	N/A	N/A	451905	451924	GCAATATTTAATTTTCTGAA	36	2178
1042306	N/A	N/A	452185	452204	TGCTGCAAATCCAAGTCATA	51	2179
1042338	N/A	N/A	452464	452483	CCTTATAGCCACTCATACAA	42	2180
1042370	N/A	N/A	452976	452995	AGTACATTCATATGGCAGCT	27	2181
1042402	N/A	N/A	453759	453778	GGCGAATTCTATATGGAGCA	98	2182
1042434	N/A	N/A	454604	454623	AACTGGATTCTCTAATTAGA	59	2183
1042466	N/A	N/A	455257	455276	GCATTCAATTTAAAAAAGGG	66	2184
1042498	N/A	N/A	456187	456206	AATAAATTTAAAAACTCTGG	108	2185
1042530	N/A	N/A	456884	456903	ATCAATATTCAAAATATTCC	89	2186

Table 30

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040099	2149	2168	436868	436887	CTGTTGCACCTCCAGGTCAG	77	2187
1040131	3050	3069	457303	457322	GCTGGCCCTTTTTAACAGAG	110	2188
1040163	3800	3819	458053	458072	CCTGTGCACCCCCACATGCG	107	2189
1040195	4416	4435	458669	458688	TGAACTATAAACAGTACTAG	69	2190
1040227	4734	4753	458987	459006	AATTCACATTCATCCCTTTA	34	2191
1040259	5079	5098	459332	459351	AACCTTATAAAATGGCCTAG	70	2192
1040291	5446	5465	459699	459718	TCTCCCTACTTATAAAACTT	31	2193
1040323	5788	5807	460041	460060	ATACAGCACTAAATAAGCAG	77	2194
1040355	6207	6226	460460	460479	GGTCAGACTCTATTGGCACA	10	2195
1040387	6987	7006	461240	461259	TTACTAGTTTAAAAATGGAA	100	2196
1040419	7414	7433	461667	461686	ACACACTCACCTAACAGAAA	68	2197
1040451	7915	7934	462168	462187	CTTCCTCACCCATATCTGAA	45	2198
1040483	8250	8269	462503	462522	GCTTTATAAAAAAGTATATT	139	2199
1040515	8600	8619	462853	462872	AGAGCCATATCTTTCAAACA	31	2200
1040547	8988	9007	463241	463260	TGTTCAAGATTATATTCTTT	73	2201
1040579	9332	9351	463585	463604	AACAGTTGCCTTCAACGAGA	29	2202
1040611	9661	9680	463914	463933	ATTACTGTAAACAACACTTC	52	2203
1040643	10205	10224	464458	464477	AACATCATTCCTTCCCTAGT	33	2204
1040675	10418	10437	464671	464690	GAGTGTATCCTACAAATAGA	53	2205
1040707	N/A	N/A	11372	11391	TCTAGCAAACCTCTTTTTCC	57	2206
1040739	N/A	N/A	27282	27301	AGGTATAAATCCCCTTTCCA	31	2207
1040771	N/A	N/A	41291	41310	GATAGTAATCAAACCTGAGT	43	2208
1040803	N/A	N/A	71489	71508	ATTTGTCTATTTTAAAGACT	117	2209
1040835	N/A	N/A	87443	87462	ATGAGTAAAATATGGTCCTT	43	2210
1040867	N/A	N/A	109082	109101	CACTTCATAATTTAATATTT	92	2211
1040899	N/A	N/A	141267	141286	GTGATATTTTAAAGACTTAC	6	2212
1040931	N/A	N/A	168114	168133	AGGGCCTTATTTTAATCACA	106	2213
1040963	N/A	N/A	188513	188532	CATTTATTTCCTTACCCAGT	6	2214
1040995	N/A	N/A	208356	208375	GTGTCTAAAACCAACTGGGT	28	2215
1041027	N/A	N/A	227703	227722	AAGCCAATATTTTATTTTGA	96	2216
1041059	N/A	N/A	251853	251872	GGTGATAAAGATATCATTAC	67	2217
1041091	N/A	N/A	270781	270800	TTCGAAATTCTTTATTTGAT	136	2218
1041123	N/A	N/A	287520	287539	CACTATAAAGAATGATGAGT	5	2219
1041155	N/A	N/A	318566	318585	TAGAGAAAACGATGTTGGCT	3	2220
1041187	N/A	N/A	339528	339547	CCTTCGGCTATTTAATAATA	75	2221
1041219	N/A	N/A	365605	365624	AGGCATCTAATTTAAATTCA	20	2222
1041251	N/A	N/A	386171	386190	GCTTGTAAAACTATGGCGGC	87	2223
1041283	N/A	N/A	413867	413886	GGCAATAAAATATTTAATGG	71	2224

1041315	N/A	N/A	437753	437772	GGGCTTATTTTTTCTAGAGA	33	2225
1041347	N/A	N/A	438223	438242	ACATTATATATATGTTGGAG	16	2226
1041379	N/A	N/A	438493	438512	ACTGGAATTATCCACTCTAA	40	2227
1041411	N/A	N/A	439103	439122	ATTGTATTAACCACGCTTTT	29	2228
1041443	N/A	N/A	439444	439463	TAGCAGCTATTTCATGACTA	15	2229
1041475	N/A	N/A	440117	440136	GTGAACAGCCACTACAGAGG	76	2230
1041507	N/A	N/A	440360	440379	CCTTCATTCTCAAGCTGAAG	88	2231
1041539	N/A	N/A	441150	441169	GATGTCAGCCGATTTCTGAT	30	2232
1041571	N/A	N/A	441554	441573	AGGCATCCTCAAGAGTCTGT	32	2233
1041603	N/A	N/A	442192	442211	GTACATGTTCATCTTAATGC	12	2234
1041635	N/A	N/A	442626	442645	GGACTCTCAACCAGAATCAA	118	2235
1041667	N/A	N/A	443027	443046	GCTGCCTCTCCTTCCATAAA	64	2236
1041699	N/A	N/A	443488	443507	CAATACATTTTACAACTCCA	27	2237
1041731	N/A	N/A	443871	443890	CTGACTCTACAGGCTCATGT	51	2238
1041763	N/A	N/A	444259	444278	CTGCTTTAAACAATAGTCTT	70	2239
1041795	N/A	N/A	445170	445189	AGGGATGGCCAGGAAGGACA	96	2240
1041827	N/A	N/A	445492	445511	ATCAGAAAACCCCGTCTCAA	104	2241
1041859	N/A	N/A	445770	445789	TCCCTGTTTTCACAAATTGC	68	2242
1041891	N/A	N/A	445980	445999	TTCAATAAAATTCCTTTCAC	93	2243
1041923	N/A	N/A	446357	446376	ATGGCCTTTATACTTTTGTA	116	2244
1041955	N/A	N/A	446849	446868	ACACATTTTCCAGAATGGTT	16	2245
1041987	N/A	N/A	447638	447657	CTTTTTTATTTACTTGTATA	80	2246
1042019	N/A	N/A	448386	448405	CACTGTCCTTTTCAGAGAGA	68	2247
1042051	N/A	N/A	448682	448701	CTTACATCACAAACATCCCA	95	2248
1042083	N/A	N/A	449050	449069	CTAATGATACATTTCAGGCT	46	2249
1042115	N/A	N/A	449593	449612	ATATATATCATCAAATCTGT	23	2250
1042147	N/A	N/A	449862	449881	CTCCTCACTAATTAGTGTGA	110	2251
1042179	N/A	N/A	450507	450526	GCCTGCCGAAAAATTCACGA	144	2252
1042211	N/A	N/A	451139	451158	CCAACCAGCCTAAAAAATTG	122	2253
1042243	N/A	N/A	451540	451559	TAGGATAATTTTATGGCACC	8	2254
1042275	N/A	N/A	451908	451927	CAGGCAATATTTAATTTTCT	11	2255
1042307	N/A	N/A	452186	452205	TTGCTGCAAATCCAAGTCAT	34	2256
1042339	N/A	N/A	452466	452485	TGCCTTATAGCCACTCATAC	33	2257
1042371	N/A	N/A	452978	452997	TGAGTACATTCATATGGCAG	13	2258
1042403	N/A	N/A	453760	453779	TGGCGAATTCTATATGGAGC	63	2259
1042435	N/A	N/A	454638	454657	AGTTGAATAGACATGGATTA	73	2260
1042467	N/A	N/A	455281	455300	ACTTTCACAATTTTGCAAAT	45	2261
1042499	N/A	N/A	456211	456230	TCTGAACAAAAATATAAGCA	106	2262
1042531	N/A	N/A	456890	456909	AAGGTCATCAATATTCAAAA	19	2263

Table 31

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040100	2215	2234	436934	436953	AGGCTTCCCTAAATGCAGGC	69	2264
1040132	3098	3117	457351	457370	GGCCGTCGGCCTTTGAGTGC	106	2265
1040164	3838	3857	458091	458110	AGGCAGAGAAAAAGAGACCC	72	2266
1040196	4421	4440	458674	458693	AGTCATGAACTATAAACAGT	34	2267
1040228	4736	4755	458989	459008	ATAATTCACATTCATCCCTT	28	2268
1040260	5084	5103	459337	459356	AACATAACCTTATAAAATGG	82	2269
1040292	5447	5466	459700	459719	TTCTCCCTACTTATAAAACT	48	2270
1040324	5798	5817	460051	460070	CGTTTAAAAAATACAGCACT	49	2271
1040356	6228	6247	460481	460500	GCTTTAACTATATAGCACAC	78	2272
1040388	6995	7014	461248	461267	GCCTGCTGTTACTAGTTTAA	31	2273
1040420	7415	7434	461668	461687	AACACACTCACCTAACAGAA	47	2274
1040452	7920	7939	462173	462192	CTCTGCTTCCTCACCCATAT	36	2275
1040484	8251	8270	462504	462523	TGCTTTATAAAAAAGTATAT	128	2276
1040516	8606	8625	462859	462878	TTCAACAGAGCCATATCTTT	65	2277
1040548	8989	9008	463242	463261	GTGTTCAAGATTATATTCTT	40	2278
1040580	9344	9363	463597	463616	GTTAGCTACCAGAACAGTTG	40	2279
1040612	9667	9686	463920	463939	GTAAGGATTACTGTAAACAA	12	2280
1040644	10208	10227	464461	464480	CAAAACATCATTCCTTCCCT	84	2281
1040676	10419	10438	464672	464691	CGAGTGTATCCTACAAATAG	56	2282
1040708	N/A	N/A	11914	11933	TGCCAGAGAATTTATATGTA	10	2283
1040740	N/A	N/A	27352	27371	CCTGTCAAAACCAGTCACTC	60	2284
1040772	N/A	N/A	41515	41534	CTAATAATAGTCTAATTACA	134	2285
1040804	N/A	N/A	71673	71692	TTGTGCTTTTAAATTCAAAC	10	2286
1040836	N/A	N/A	87528	87547	ACATCCTTTTAAATGTTAGG	31	2287
1040868	N/A	N/A	109301	109320	TGTCTTAATCAAACCTCCCG	50	2288
1040900	N/A	N/A	141437	141456	CAGTTCTATTTTTAGTTATA	10	2289
1040932	N/A	N/A	168436	168455	ATTTACCTTCTTTAACACAA	66	2290
1040964	N/A	N/A	188787	188806	GGGATATTTTAAAATTCTAC	54	2291
1040996	N/A	N/A	208934	208953	CCTGGGTTTCAAAGATTCCT	100	2292
1041028	N/A	N/A	229640	229659	TAGAGAATTCAAAGCACCAA	46	2293
1041060	N/A	N/A	253001	253020	TCAAAGTTTTAAAGAGTTTT	88	2294
1041092	N/A	N/A	271090	271109	TGCTCCAAACCCAGCTCCTC	132	2295
1041124	N/A	N/A	288911	288930	CCCTACTCCTTTTATAGATG	32	2296
1041156	N/A	N/A	319014	319033	TCATCCAAACCCAGACGGGT	120	2297
1041188	N/A	N/A	339984	340003	ATAAAGTCCTTTTAACCCCT	4	2298
1041220	N/A	N/A	367208	367227	GTGCCCTTTTAAAATCTTTT	6	2299
1041252	N/A	N/A	386698	386717	AGCCAAAAATACATCCACCT	24	2300
1041284	N/A	N/A	413882	413901	ACTGTAATCTAAACAGGCAA	87	2301

1041316	N/A	N/A	437786	437805	TTCATTACACACAGCAGAGA	26	2302
1041348	N/A	N/A	438225	438244	AGACATTATATATATGTTGG	27	2303
1041380	N/A	N/A	438512	438531	CCCCTACACCCCAGAGCACA	109	2304
1041412	N/A	N/A	439104	439123	GATTGTATTAACCACGCTTT	18	2305
1041444	N/A	N/A	439457	439476	TGAATGTCCCAAATAGCAGC	34	2306
1041476	N/A	N/A	440138	440157	CACCCCTAATTCATGCAGGA	72	2307
1041508	N/A	N/A	440361	440380	GCCTTCATTCTCAAGCTGAA	43	2308
1041540	N/A	N/A	441162	441181	TTTAGCTGTGATGATGTCAG	51	2309
1041572	N/A	N/A	441556	441575	TCAGGCATCCTCAAGAGTCT	68	2310
1041604	N/A	N/A	442235	442254	CTTTAGTTCCCATGAGGTCT	41	2311
1041636	N/A	N/A	442680	442699	AAGTGGATTATATTTGGCAG	7	2312
1041668	N/A	N/A	443031	443050	ATCAGCTGCCTCTCCTTCCA	47	2313
1041700	N/A	N/A	443489	443508	CCAATACATTTTACAACTCC	57	2314
1041732	N/A	N/A	443874	443893	GGACTGACTCTACAGGCTCA	41	2315
1041764	N/A	N/A	444260	444279	ACTGCTTTAAACAATAGTCT	65	2316
1041796	N/A	N/A	445235	445254	TTTTTCTTACACATGGTAGC	28	2317
1041828	N/A	N/A	445506	445525	TCAGCATGAAAAAAATCAGA	76	2318
1041860	N/A	N/A	445772	445791	AGTCCCTGTTTTCACAAATT	45	2319
1041892	N/A	N/A	446016	446035	GCTTTTAAGAAAAATTTTAG	123	2320
1041924	N/A	N/A	446359	446378	GGATGGCCTTTATACTTTTG	52	2321
1041956	N/A	N/A	446875	446894	TCATTTTATGATCTTGCTGG	25	2322
1041988	N/A	N/A	447659	447678	CTGGTTATCTTCTTATGCAT	89	2323
1042020	N/A	N/A	448422	448441	TTTGGAATCTTTTTTGCCTC	44	2324
1042052	N/A	N/A	448684	448703	CTCTTACATCACAAACATCC	102	2325
1042084	N/A	N/A	449054	449073	GTTCCTAATGATACATTTCA	52	2326
1042116	N/A	N/A	449594	449613	AATATATATCATCAAATCTG	46	2327
1042148	N/A	N/A	449866	449885	TTTTCTCCTCACTAATTAGT	112	2328
1042180	N/A	N/A	450508	450527	AGCCTGCCGAAAAATTCACG	116	2329
1042212	N/A	N/A	451152	451171	CCATAAAAACCCTCCAACCA	112	2330
1042244	N/A	N/A	451541	451560	CTAGGATAATTTTATGGCAC	9	2331
1042276	N/A	N/A	451909	451928	GCAGGCAATATTTAATTTTC	37	2332
1042308	N/A	N/A	452218	452237	GGAAACCAATCCCACATCAA	78	2333
1042340	N/A	N/A	452472	452491	AGTGTTTGCCTTATAGCCAC	20	2334
1042372	N/A	N/A	452979	452998	TTGAGTACATTCATATGGCA	30	2335
1042404	N/A	N/A	453783	453802	TGCTAAAGAAAAAGAATTGT	111	2336
1042436	N/A	N/A	454643	454662	TTTCCAGTTGAATAGACATG	62	2337
1042468	N/A	N/A	455285	455304	AATTACTTTCACAATTTTGC	27	2338
1042500	N/A	N/A	456212	456231	CTCTGAACAAAAATATAAGC	87	2339
1042532	N/A	N/A	456957	456976	ACACACTATAAATGAGGCTC	46	2340

Table 32

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040101	2216	2235	436935	436954	CAGGCTTCCCTAAATGCAGG	70	2341
1040133	3109	3128	457362	457381	GCTGCCCGCCAGGCCGTCGG	111	2342
1040165	3880	3899	458133	458152	CCCCCCCGGCCCATGCCGAT	108	2343
1040197	4422	4441	458675	458694	TAGTCATGAACTATAAACAG	46	2344
1040229	4738	4757	458991	459010	TCATAATTCACATTCATCCC	16	2345
1040261	5106	5125	459359	459378	GACCAAAATGAATTTTCAAA	26	2346
1040293	5458	5477	459711	459730	TATTTAAAAATTTCTCCCTA	95	2347
1040325	5902	5921	460155	460174	TCTTACCATCAAAGGCTAAA	60	2348
1040357	6229	6248	460482	460501	AGCTTTAACTATATAGCACA	107	2349
1040389	7040	7059	461293	461312	CCTGACTAATTTCTTGGTGA	46	2350
1040421	7422	7441	461675	461694	AAAACCCAACACACTCACCT	116	2351
1040453	7964	7983	462217	462236	GACAACCAACACAGCTCAAG	83	2352
1040485	8252	8271	462505	462524	GTGCTTTATAAAAAAGTATA	94	2353
1040517	8613	8632	462866	462885	TCATTGTTTCAACAGAGCCA	12	2354
1040549	8990	9009	463243	463262	CGTGTTCAAGATTATATTCT	49	2355
1040581	9345	9364	463598	463617	AGTTAGCTACCAGAACAGTT	52	2356
1040613	9711	9730	463964	463983	TGTCACCTAATACTTGGTAT	25	2357
1040645	10211	10230	464464	464483	GTGCAAAACATCATTCCTTC	10	2358
1040677	10436	10455	464689	464708	AATTCAATAAACAGACTCGA	40	2359
1040709	N/A	N/A	12342	12361	TTCAGAATTTAAAATTCAGC	15	2360
1040741	N/A	N/A	27434	27453	ACAATTAGCCAAAACTGAAT	45	2361
1040773	N/A	N/A	42923	42942	CGTTCCAAATTATTCCTGCT	7	2362
1040805	N/A	N/A	72788	72807	ATTTGCTCCTTTTATCATTG	7	2363
1040837	N/A	N/A	87598	87617	ACATTATTTCAAAACCCACA	49	2364
1040869	N/A	N/A	110925	110944	TAGTGGTTAGATTAACAGCT	6	2365
1040901	N/A	N/A	141588	141607	GTCTCATAACGATAACCAAA	23	2366
1040933	N/A	N/A	169799	169818	ACCTTTAAAATTTTTTCAGC	94	2367
1040965	N/A	N/A	189270	189289	GCTTACAAAGCCATAGAACC	67	2368
1040997	N/A	N/A	209089	209108	GTCTACAGCCTTTAACGACT	85	2369
1041029	N/A	N/A	229753	229772	CCAGTTAACCAAAAAATTTT	119	2370
1041061	N/A	N/A	255397	255416	GGCTACTATCAAATACATTT	9	2371
1041093	N/A	N/A	271117	271136	TGTTTATTTCAAACTTTCCC	55	2372
1041125	N/A	N/A	289433	289452	GGTCTTGGCCCTTAACTGTT	20	2373
1041157	N/A	N/A	319225	319244	CCCTGATAAATTTATGAATT	50	2374
1041189	N/A	N/A	341174	341193	TTTGATCTGCCTTATCTCTG	14	2375
1041221	N/A	N/A	367501	367520	TTTGTATTTTAAACTGAGTG	5	2376
1041253	N/A	N/A	386699	386718	AAGCCAAAAATACATCCACC	46	2377
1041285	N/A	N/A	414009	414028	CTTTTTAGAATACCATGCCC	95	2378

1041317	N/A	N/A	437788	437807	AATTCATTACACACAGCAGA	8	2379
1041349	N/A	N/A	438226	438245	AAGACATTATATATATGTTG	89	2380
1041381	N/A	N/A	438520	438539	AAGGACAGCCCCTACACCCC	97	2381
1041413	N/A	N/A	439106	439125	CAGATTGTATTAACCACGCT	5	2382
1041445	N/A	N/A	439471	439490	TGTTTTATTTTATCTGAATG	61	2383
1041477	N/A	N/A	440139	440158	CCACCCCTAATTCATGCAGG	67	2384
1041509	N/A	N/A	440364	440383	GCTGCCTTCATTCTCAAGCT	81	2385
1041541	N/A	N/A	441172	441191	GGTGGAGTATTTTAGCTGTG	10	2386
1041573	N/A	N/A	441564	441583	TTATGAGTTCAGGCATCCTC	15	2387
1041605	N/A	N/A	442237	442256	GGCTTTAGTTCCCATGAGGT	20	2388
1041637	N/A	N/A	442682	442701	TTAAGTGGATTATATTTGGC	11	2389
1041669	N/A	N/A	443041	443060	CTAGACTTTCATCAGCTGCC	53	2390
1041701	N/A	N/A	443490	443509	ACCAATACATTTTACAACTC	34	2391
1041733	N/A	N/A	443877	443896	AAGGGACTGACTCTACAGGC	16	2392
1041765	N/A	N/A	444289	444308	GACCTCTCTCTACTTGCTGT	30	2393
1041797	N/A	N/A	445239	445258	TGGGTTTTTCTTACACATGG	9	2394
1041829	N/A	N/A	445574	445593	GTCTTGTTTTACCTGTAGAG	6	2395
1041861	N/A	N/A	445787	445806	CATTTCCTTCACAAGAGTCC	78	2396
1041893	N/A	N/A	446036	446055	CCTAATCTGACTAATGACTG	94	2397
1041925	N/A	N/A	446361	446380	AGGGATGGCCTTTATACTTT	46	2398
1041957	N/A	N/A	446885	446904	AATCATTAAGTCATTTTATG	79	2399
1041989	N/A	N/A	447660	447679	ACTGGTTATCTTCTTATGCA	120	2400
1042021	N/A	N/A	448436	448455	ACTCTCTCCATTCATTTGGA	52	2401
1042053	N/A	N/A	448685	448704	TCTCTTACATCACAAACATC	94	2402
1042085	N/A	N/A	449059	449078	TGAGGGTTCCTAATGATACA	41	2403
1042117	N/A	N/A	449599	449618	GTGAGAATATATATCATCAA	100	2404
1042149	N/A	N/A	449885	449904	CTTGCCAGCCCAATGCTAGT	95	2405
1042181	N/A	N/A	450520	450539	CATAGCTAGAACAGCCTGCC	107	2406
1042213	N/A	N/A	451153	451172	CCCATAAAAACCCTCCAACC	102	2407
1042245	N/A	N/A	451542	451561	GCTAGGATAATTTTATGGCA	40	2408
1042277	N/A	N/A	451926	451945	TATACACACTTCACAGGGCA	56	2409
1042309	N/A	N/A	452223	452242	CAGAAGGAAACCAATCCCAC	80	2410
1042341	N/A	N/A	452473	452492	CAGTGTTTGCCTTATAGCCA	11	2411
1042373	N/A	N/A	452982	453001	AACTTGAGTACATTCATATG	72	2412
1042405	N/A	N/A	453799	453818	TGGAATATCTTTACAGTGCT	38	2413
1042437	N/A	N/A	454668	454687	CACTGAAATCAAGAATGCAA	81	2414
1042469	N/A	N/A	455287	455306	TGAATTACTTTCACAATTTT	73	2415
1042501	N/A	N/A	456214	456233	AACTCTGAACAAAAATATAA	151	2416
1042533	N/A	N/A	456961	456980	AGCCACACACTATAAATGAG	99	2417

Table 33

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040102	2217	2236	436936	436955	CCAGGCTTCCCTAAATGCAG	92	2418
1040134	3141	3160	457394	457413	ATTCCGTTTTCCTGCTCGGC	32	2419
1040166	3890	3909	458143	458162	CTGCTCTGAACCCCCCCGGC	100	2420
1040198	4429	4448	458682	458701	TTGTCCATAGTCATGAACTA	78	2421
1040230	4739	4758	458992	459011	TTCATAATTCACATTCATCC	10	2422
1040262	5119	5138	459372	459391	GATGTGGTAAAAAGACCAAA	38	2423
1040294	5459	5478	459712	459731	ATATTTAAAAATTTCTCCCT	90	2424
1040326	5904	5923	460157	460176	CCTCTTACCATCAAAGGCTA	57	2425
1040358	6230	6249	460483	460502	GAGCTTTAACTATATAGCAC	44	2426
1040390	7045	7064	461298	461317	TTCGCCCTGACTAATTTCTT	25	2427
1040422	7450	7469	461703	461722	GGATGCTGCCACTTCCTGGT	66	2428
1040454	7968	7987	462221	462240	CCATGACAACCAACACAGCT	131	2429
1040486	8278	8297	462531	462550	CCAACCCAACACAATAGCAG	33	2430
1040518	8615	8634	462868	462887	ACTCATTGTTTCAACAGAGC	27	2431
1040550	9008	9027	463261	463280	CCCTTGTTACAAACACTTCG	65	2432
1040582	9369	9388	463622	463641	CCCTCCCGCCATTACACAGG	83	2433
1040614	9714	9733	463967	463986	TAGTGTCACCTAATACTTGG	59	2434
1040646	10212	10231	464465	464484	GGTGCAAAACATCATTCCTT	21	2435
1040678	10442	10461	464695	464714	CCATAAAATTCAATAAACAG	108	2436
1040710	N/A	N/A	13427	13446	ATAAGCTTTCTTTAAATGCA	9	2437
1040742	N/A	N/A	27656	27675	GTGTTCTTTCTTTAACAGTT	4	2438
1040774	N/A	N/A	42927	42946	CCCCCGTTCCAAATTATTCC	106	2439
1040806	N/A	N/A	74008	74027	GTTTTTATCCATTACAAGAG	22	2440
1040838	N/A	N/A	88730	88749	ACCCGCAATCAAATACTGCC	73	2441
1040870	N/A	N/A	111213	111232	CTAATGTGCCCTTAACATGG	95	2442
1040902	N/A	N/A	141663	141682	GCTCATAAAACCATGTGCTC	100	2443
1040934	N/A	N/A	170327	170346	GCTTGATTTTAAACTTTATA	40	2444
1040966	N/A	N/A	190544	190563	ACCCTCAAACGAATAGGCTC	145	2445
1040998	N/A	N/A	209796	209815	TCCACACAAGAATAATCTAC	86	2446
1041030	N/A	N/A	230401	230420	GCTAGGAAAATTTACCATAC	29	2447
1041062	N/A	N/A	255626	255645	GATTAAATAATTTAAGCACA	110	2448
1041094	N/A	N/A	271334	271353	TCTTGGGTTCCTTATATTAC	56	2449
1041126	N/A	N/A	290352	290371	TAGGTGTTTATTTAGAACCC	12	2450
1041158	N/A	N/A	319445	319464	TCATGCTTTCAAAACACAGT	11	2451
1041190	N/A	N/A	342628	342647	AATGAAATCATTTACTGAAC	85	2452
1041222	N/A	N/A	368463	368482	AGTGTAATACATTACTCATA	5	2453
1041254	N/A	N/A	387051	387070	GTATACAAAGATATAACCTG	76	2454
1041286	N/A	N/A	418439	418458	TGTTTGTTTTAAAATTAGGG	72	2455

1041318	N/A	N/A	437792	437811	GGTTAATTCATTACACACAG	3	2456
1041350	N/A	N/A	438237	438256	ACCTAAATAATAAGACATTA	141	2457
1041382	N/A	N/A	438532	438551	AGCCAGACAACTAAGGACAG	80	2458
1041414	N/A	N/A	439107	439126	TCAGATTGTATTAACCACGC	5	2459
1041446	N/A	N/A	439472	439491	TTGTTTTATTTTATCTGAAT	95	2460
1041478	N/A	N/A	440143	440162	GTACCCACCCCTAATTCATG	119	2461
1041510	N/A	N/A	440366	440385	TGGCTGCCTTCATTCTCAAG	106	2462
1041542	N/A	N/A	441188	441207	TGTGGCAAACACAGCTGGTG	45	2463
1041574	N/A	N/A	441611	441630	ATACTATATCACACTGCTTT	58	2464
1041606	N/A	N/A	442251	442270	GTTTTATATGCCATGGCTTT	58	2465
1041638	N/A	N/A	442691	442710	TGGAGGATATTAAGTGGATT	22	2466
1041670	N/A	N/A	443042	443061	TCTAGACTTTCATCAGCTGC	66	2467
1041702	N/A	N/A	443492	443511	TTACCAATACATTTTACAAC	72	2468
1041734	N/A	N/A	443917	443936	GGCATGTTCAATGTTGGCAA	16	2469
1041766	N/A	N/A	444314	444333	ACAGGGAAAACTGTTAGGTG	7	2470
1041798	N/A	N/A	445240	445259	CTGGGTTTTTCTTACACATG	10	2471
1041830	N/A	N/A	445576	445595	CAGTCTTGTTTTACCTGTAG	6	2472
1041862	N/A	N/A	445791	445810	CTCCCATTTCCTTCACAAGA	53	2473
1041894	N/A	N/A	446044	446063	GTCACCTTCCTAATCTGACT	106	2474
1041926	N/A	N/A	446679	446698	CCTTTATAACTTTTCTTTCT	28	2475
1041958	N/A	N/A	446891	446910	GTTAGTAATCATTAAGTCAT	5	2476
1041990	N/A	N/A	447677	447696	CCCTGGTGCCAAAAGGGACT	100	2477
1042022	N/A	N/A	448475	448494	TCTTTAACCCCTCTTGCGCC	123	2478
1042054	N/A	N/A	448687	448706	TTTCTCTTACATCACAAACA	116	2479
1042086	N/A	N/A	449060	449079	TTGAGGGTTCCTAATGATAC	54	2480
1042118	N/A	N/A	449600	449619	AGTGAGAATATATATCATCA	122	2481
1042150	N/A	N/A	449916	449935	AATCTGATCATTGTAGGCAC	12	2482
1042182	N/A	N/A	450530	450549	TGGTGTGAACCATAGCTAGA	120	2483
1042214	N/A	N/A	451161	451180	ACCCCCCTCCCATAAAAACC	117	2484
1042246	N/A	N/A	451566	451585	GGTTTTACCCTTTCCTGCAC	90	2485
1042278	N/A	N/A	451931	451950	CACATTATACACACTTCACA	78	2486
1042310	N/A	N/A	452244	452263	TCATTAACAACATAAACTGA	74	2487
1042342	N/A	N/A	452495	452514	CATGGTACAGATAATTGTGA	57	2488
1042374	N/A	N/A	453018	453037	TACTGGATCCATACAAGGCA	33	2489
1042406	N/A	N/A	453800	453819	ATGGAATATCTTTACAGTGC	17	2490
1042438	N/A	N/A	454669	454688	CCACTGAAATCAAGAATGCA	121	2491
1042470	N/A	N/A	455290	455309	TCTTGAATTACTTTCACAAT	24	2492
1042502	N/A	N/A	456227	456246	GAGGACAACTAAAAACTCTG	105	2493
1042534	N/A	N/A	456962	456981	CAGCCACACACTATAAATGA	112	2494

Table 34

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040103	2218	2237	436937	436956	GCCAGGCTTCCCTAAATGCA	135	2495
1040135	3180	3199	457433	457452	TCGCCATTCTCAGAGAGCAT	79	2496
1040167	3909	3928	458162	458181	TGGGAACCCCAGGAGGACAC	54	2497
1040199	4484	4503	458737	458756	ATCTAATTCCTCATGTCACA	15	2498
1040231	4740	4759	458993	459012	GTTCATAATTCACATTCATC	8	2499
1040263	5161	5180	459414	459433	CAGAGTTTCTAAGAGCCCGC	38	2500
1040295	5460	5479	459713	459732	AATATTTAAAAATTTCTCCC	110	2501
1040327	5906	5925	460159	460178	TTCCTCTTACCATCAAAGGC	38	2502
1040359	6232	6251	460485	460504	ATGAGCTTTAACTATATAGC	31	2503
1040391	7049	7068	461302	461321	TCTTTTCGCCCTGACTAATT	32	2504
1040423	7495	7514	461748	461767	AAGAGGTGTGAAAGGTTCCG	27	2505
1040455	7969	7988	462222	462241	GCCATGACAACCAACACAGC	96	2506
1040487	8283	8302	462536	462555	GGAAACCAACCCAACACAAT	73	2507
1040519	8662	8681	462915	462934	ACTTTCAACCCTTCTCTGCT	53	2508
1040551	9010	9029	463263	463282	ATCCCTTGTTACAAACACTT	33	2509
1040583	9370	9389	463623	463642	TCCCTCCCGCCATTACACAG	94	2510
1040615	9719	9738	463972	463991	TGAGCTAGTGTCACCTAATA	12	2511
1040647	10213	10232	464466	464485	AGGTGCAAAACATCATTCCT	36	2512
1040679	10447	10466	464700	464719	AGGGACCATAAAATTCAATA	22	2513
1040711	N/A	N/A	14141	14160	CTCCTCCAAATTTATCTTCA	56	2514
1040743	N/A	N/A	28302	28321	CACAAAATACATTAAGTCCT	27	2515
1040775	N/A	N/A	43117	43136	TCCAGCAAAATATTTCTTTA	39	2516
1040807	N/A	N/A	74082	74101	TTGATCAACCAAAGATGGCT	39	2517
1040839	N/A	N/A	88777	88796	CCAATGGCTTTTTAACAGAT	27	2518
1040871	N/A	N/A	112988	113007	AACACATTAGATTATGAGTA	11	2519
1040903	N/A	N/A	141741	141760	AGGGTGTTATTTTAGAGTAA	13	2520
1040935	N/A	N/A	171157	171176	GCTGGAAAAGAATCTGAGCA	114	2521
1040967	N/A	N/A	190616	190635	GTTATATTATTTTATCCCTT	14	2522
1040999	N/A	N/A	209931	209950	GAAGATATCTTTTATGACAC	23	2523
1041031	N/A	N/A	231711	231730	CACAGTAGCCAAAAGCAGTC	95	2524
1041063	N/A	N/A	255652	255671	GTATATATTATTTAAAATGT	101	2525
1041095	N/A	N/A	273041	273060	AGCTGGTTTCTTTAGCCACC	81	2526
1041127	N/A	N/A	290740	290759	GACTGAAAAATACCCAGCCA	102	2527
1041159	N/A	N/A	322660	322679	TAGGCCTTATTTTATTCCAT	72	2528
1041191	N/A	N/A	342814	342833	TGAGCTTTTTAAAAACAGTT	4	2529
1041223	N/A	N/A	369251	369270	TTTCTTAGCCAAAGAGATAT	85	2530
1041255	N/A	N/A	387144	387163	TGTTCAATTTAAAAGCCTTG	5	2531
1041287	N/A	N/A	418795	418814	ATCTGCAAAGAATCTGCCCC	72	2532

1041319	N/A	N/A	437793	437812	AGGTTAATTCATTACACACA	5	2533
1041351	N/A	N/A	438241	438260	TCATACCTAAATAATAAGAC	102	2534
1041383	N/A	N/A	438533	438552	CAGCCAGACAACTAAGGACA	57	2535
1041415	N/A	N/A	439116	439135	CCTGACTTCTCAGATTGTAT	50	2536
1041447	N/A	N/A	439505	439524	ATTCAAACCATTAATTAGTT	73	2537
1041479	N/A	N/A	440144	440163	AGTACCCACCCCTAATTCAT	98	2538
1041511	N/A	N/A	440368	440387	AGTGGCTGCCTTCATTCTCA	52	2539
1041543	N/A	N/A	441206	441225	GACTCTGAACCTGTCACTTG	83	2540
1041575	N/A	N/A	441613	441632	CCATACTATATCACACTGCT	21	2541
1041607	N/A	N/A	442255	442274	CTCAGTTTTATATGCCATGG	44	2542
1041639	N/A	N/A	442692	442711	TTGGAGGATATTAAGTGGAT	14	2543
1041671	N/A	N/A	443043	443062	TTCTAGACTTTCATCAGCTG	102	2544
1041703	N/A	N/A	443494	443513	CTTTACCAATACATTTTACA	61	2545
1041735	N/A	N/A	443936	443955	ATTCATCGCCACCAAGCTCG	48	2546
1041767	N/A	N/A	444343	444362	ATCTATCACACCAATGCAAG	29	2547
1041799	N/A	N/A	445241	445260	GCTGGGTTTTTCTTACACAT	25	2548
1041831	N/A	N/A	445587	445606	AGTGAAATTCTCAGTCTTGT	37	2549
1041863	N/A	N/A	445806	445825	GTTGTTTAAATATGTCTCCC	8	2550
1041895	N/A	N/A	446045	446064	TGTCACCTTCCTAATCTGAC	51	2551
1041927	N/A	N/A	446680	446699	GCCTTTATAACTTTTCTTTC	11	2552
1041959	N/A	N/A	446892	446911	TGTTAGTAATCATTAAGTCA	12	2553
1041991	N/A	N/A	447705	447724	CCAAAAAATCTTCTTCCATG	45	2554
1042023	N/A	N/A	448476	448495	TTCTTTAACCCCTCTTGCGC	94	2555
1042055	N/A	N/A	448712	448731	CTTGGAATCATACTTTCTTC	55	2556
1042087	N/A	N/A	449061	449080	ATTGAGGGTTCCTAATGATA	46	2557
1042119	N/A	N/A	449602	449621	TCAGTGAGAATATATATCAT	98	2558
1042151	N/A	N/A	449921	449940	CAGATAATCTGATCATTGTA	45	2559
1042183	N/A	N/A	450531	450550	GTGGTGTGAACCATAGCTAG	97	2560
1042215	N/A	N/A	451169	451188	CCCCCCATACCCCCCTCCCA	92	2561
1042247	N/A	N/A	451567	451586	GGGTTTTACCCTTTCCTGCA	99	2562
1042279	N/A	N/A	451933	451952	GCCACATTATACACACTTCA	13	2563
1042311	N/A	N/A	452245	452264	GTCATTAACAACATAAACTG	21	2564
1042343	N/A	N/A	452496	452515	CCATGGTACAGATAATTGTG	105	2565
1042375	N/A	N/A	453045	453064	CTGATACATTTCTAGAATGA	28	2566
1042407	N/A	N/A	453852	453871	TCACAGTTTACATCTCAACA	28	2567
1042439	N/A	N/A	454686	454705	TAGAATTAAAATATACACCA	69	2568
1042471	N/A	N/A	455291	455310	GTCTTGAATTACTTTCACAA	9	2569
1042503	N/A	N/A	456245	456264	TGGACCAACCCTCCTTCTGA	81	2570
1042535	N/A	N/A	456967	456986	TCCCCCAGCCACACACTATA	102	2571

Table 35

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	1	138
1040104	2348	2367	437067	437086	TCAGGTAGCCGATGACAGGG	44	2572
1040136	3181	3200	457434	457453	TTCGCCATTCTCAGAGAGCA	57	2573
1040168	3937	3956	458190	458209	GCTGGGTTCCTGATGTTGAT	31	2574
1040200	4485	4504	458738	458757	AATCTAATTCCTCATGTCAC	21	2575
1040232	4741	4760	458994	459013	AGTTCATAATTCACATTCAT	13	2576
1040264	5162	5181	459415	459434	TCAGAGTTTCTAAGAGCCCG	17	2577
1040296	5477	5496	459730	459749	GCAGCCATCCAAGTAAGAAT	16	2578
1040328	5913	5932	460166	460185	GCCCGTATTCCTCTTACCAT	12	2579
1040360	6268	6287	460521	460540	GGAAGATCAACCAAACAAGG	46	2580
1040392	7061	7080	461314	461333	GTATTATTTTTTTCTTTTCG	11	2581
1040424	7563	7582	461816	461835	CAGAGCAGTCAAAGTGCTGC	118	2582
1040456	7970	7989	462223	462242	AGCCATGACAACCAACACAG	63	2583
1040488	8289	8308	462542	462561	AAGAGAGGAAACCAACCCAA	50	2584
1040520	8663	8682	462916	462935	AACTTTCAACCCTTCTCTGC	37	2585
1040552	9040	9059	463293	463312	ATAATGAGTCCTGTTTGATT	20	2586
1040584	9377	9396	463630	463649	CCGGTGTTCCCTCCCGCCAT	85	2587
1040616	9772	9791	464025	464044	CAGAGAAAACCTGTGCACCG	71	2588
1040648	10214	10233	464467	464486	AAGGTGCAAAACATCATTCC	35	2589
1040680	10463	10482	464716	464735	AAGCACCATCAAAGAAAGGG	24	2590
1040712	N/A	N/A	14174	14193	ACCCAATTTCAAAGATCACT	29	2591
1040744	N/A	N/A	28305	28324	GTTCACAAAATACATTAAGT	6	2592
1040776	N/A	N/A	43918	43937	AGATCAATTCAAAGGCTCCT	62	2593
1040808	N/A	N/A	74369	74388	GATTTGTATTTTTAATTGAC	58	2594
1040840	N/A	N/A	89862	89881	TTGACATTTTAAAACAGCTC	40	2595
1040872	N/A	N/A	114285	114304	AAGCTTATCCAAAAACATTT	70	2596
1040904	N/A	N/A	143859	143878	CCCCTCAACCAAACTTTTAC	116	2597
1040936	N/A	N/A	172540	172559	TATTAATTTCATTACCATGA	92	2598
1040968	N/A	N/A	190768	190787	CCTAGAATACATTATTCCTC	56	2599
1041000	N/A	N/A	209947	209966	AGCATATTTTAAAGAAGAAG	76	2600
1041032	N/A	N/A	233011	233030	GTCCATACACCTTAATAAGT	29	2601
1041064	N/A	N/A	256096	256115	GATTACTTTTAAAAGCAACA	54	2602
1041096	N/A	N/A	273624	273643	CCTAAAAGAATTTATCCATA	96	2603
1041128	N/A	N/A	290841	290860	CTTGGCAAATTATTATCTGC	12	2604
1041160	N/A	N/A	322672	322691	GCTAAGAAAATATAGGCCTT	73	2605
1041192	N/A	N/A	343258	343277	GGCTTTATAGTCTAAGTTGC	7	2606
1041224	N/A	N/A	369453	369472	ACTTCAAACCTTTATCAGTT	3	2607
1041256	N/A	N/A	388260	388279	CAAACCCAAATTTAGCTCTG	41	2608
1041288	N/A	N/A	420471	420490	CCTTTAAGCCCTTAAAGCTG	110	2609

1041320	N/A	N/A	437794	437813	GAGGTTAATTCATTACACAC	5	2610
1041352	N/A	N/A	438248	438267	GGCCTTATCATACCTAAATA	61	2611
1041384	N/A	N/A	438538	438557	ACCAGCAGCCAGACAACTAA	66	2612
1041416	N/A	N/A	439148	439167	TACCCCAAGCCCAGCAGGTC	108	2613
1041448	N/A	N/A	439513	439532	CCAAAACAATTCAAACCATT	40	2614
1041480	N/A	N/A	440152	440171	TTTCTCCTAGTACCCACCCC	78	2615
1041512	N/A	N/A	440369	440388	AAGTGGCTGCCTTCATTCTC	44	2616
1041544	N/A	N/A	441287	441306	GGAACCTCAATTAAGTCCAG	38	2617
1041576	N/A	N/A	441615	441634	CACCATACTATATCACACTG	29	2618
1041608	N/A	N/A	442256	442275	CCTCAGTTTTATATGCCATG	6	2619
1041640	N/A	N/A	442706	442725	TTATGGCCTCAAACTTGGAG	53	2620
1041672	N/A	N/A	443046	443065	TCTTTCTAGACTTTCATCAG	33	2621
1041704	N/A	N/A	443496	443515	CACTTTACCAATACATTTTA	80	2622
1041736	N/A	N/A	443941	443960	TTAGGATTCATCGCCACCAA	19	2623
1041768	N/A	N/A	444346	444365	CCAATCTATCACACCAATGC	24	2624
1041800	N/A	N/A	445254	445273	TCCCACATTAAAAGCTGGGT	109	2625
1041832	N/A	N/A	445593	445612	TCTGCAAGTGAAATTCTCAG	66	2626
1041864	N/A	N/A	445849	445868	GTACATATCACCAAAAACAA	57	2627
1041896	N/A	N/A	446046	446065	ATGTCACCTTCCTAATCTGA	26	2628
1041928	N/A	N/A	446684	446703	AATAGCCTTTATAACTTTTC	18	2629
1041960	N/A	N/A	446894	446913	TGTGTTAGTAATCATTAAGT	19	2630
1041992	N/A	N/A	447708	447727	CTGCCAAAAAATCTTCTTCC	50	2631
1042024	N/A	N/A	448482	448501	TGCTGGTTCTTTAACCCCTC	40	2632
1042056	N/A	N/A	448729	448748	GCTGTTCAATCAAGCACCTT	76	2633
1042088	N/A	N/A	449072	449091	CTCAAAATATTATTGAGGGT	35	2634
1042120	N/A	N/A	449604	449623	TCTCAGTGAGAATATATATC	103	2635
1042152	N/A	N/A	449922	449941	TCAGATAATCTGATCATTGT	54	2636
1042184	N/A	N/A	450547	450566	CTTAGAATTAAATGCTGTGG	63	2637
1042216	N/A	N/A	451173	451192	GTCTCCCCCCATACCCCCCT	81	2638
1042248	N/A	N/A	451670	451689	AACTCCAAAGACACCACTCT	86	2639
1042280	N/A	N/A	451934	451953	AGCCACATTATACACACTTC	16	2640
1042312	N/A	N/A	452252	452271	TCTTAGAGTCATTAACAACA	15	2641
1042344	N/A	N/A	452506	452525	TGGGCTTGTTCCATGGTACA	42	2642
1042376	N/A	N/A	453046	453065	TCTGATACATTTCTAGAATG	36	2643
1042408	N/A	N/A	453854	453873	ACTCACAGTTTACATCTCAA	16	2644
1042440	N/A	N/A	454687	454706	GTAGAATTAAAATATACACC	17	2645
1042472	N/A	N/A	455293	455312	AGGTCTTGAATTACTTTCAC	7	2646
1042504	N/A	N/A	456246	456265	TTGGACCAACCCTCCTTCTG	114	2647
1042536	N/A	N/A	456983	457002	TTTGCAAACCTCCCTCTCCC	106	2648

Table 36

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040105	2350	2369	437069	437088	GCTCAGGTAGCCGATGACAG	84	2649
1040137	3185	3204	457438	457457	TCAGTTCGCCATTCTCAGAG	68	2650
1040169	3938	3957	458191	458210	AGCTGGGTTCCTGATGTTGA	45	2651
1040201	4488	4507	458741	458760	CAAAATCTAATTCCTCATGT	61	2652
1040233	4742	4761	458995	459014	TAGTTCATAATTCACATTCA	19	2653
1040265	5163	5182	459416	459435	CTCAGAGTTTCTAAGAGCCC	27	2654
1040297	5481	5500	459734	459753	AGTTGCAGCCATCCAAGTAA	26	2655
1040329	5914	5933	460167	460186	AGCCCGTATTCCTCTTACCA	22	2656
1040361	6269	6288	460522	460541	GGGAAGATCAACCAAACAAG	37	2657
1040393	7076	7095	461329	461348	GGTTTCTTATTAATAGTATT	23	2658
1040425	7575	7594	461828	461847	ACAACCCTACTCCAGAGCAG	59	2659
1040457	7976	7995	462229	462248	AACAGTAGCCATGACAACCA	80	2660
1040489	8317	8336	462570	462589	TGCCAGAAACACAACACTGT	88	2661
1040521	8668	8687	462921	462940	CATGTAACTTTCAACCCTTC	28	2662
1040553	9050	9069	463303	463322	TTTTGTCCCCATAATGAGTC	47	2663
1040585	9393	9412	463646	463665	ACATGAAAAACTGAAGCCGG	67	2664
1040617	9815	9834	464068	464087	CCTGGGCCAGAAAACTGAAA	131	2665
1040649	10226	10245	464479	464498	TTTCTTTTCAATAAGGTGCA	14	2666
1040681	10476	10495	464729	464748	CTAGAAAACCTGCAAGCACC	32	2667
1040713	N/A	N/A	14562	14581	GCTGAATTTCAAACGCAGCA	96	2668
1040745	N/A	N/A	28358	28377	GCAGTAATTTAAAGTATGAA	35	2669
1040777	N/A	N/A	44806	44825	AACAAATTTTAAAGCTCTTT	36	2670
1040809	N/A	N/A	75467	75486	AGCATCAACCAAATTCAGTA	20	2671
1040841	N/A	N/A	91912	91931	CCCTGACCTATTTAACATAC	135	2672
1040873	N/A	N/A	114340	114359	CTGTTTAACCAAAAACATCT	85	2673
1040905	N/A	N/A	144629	144648	ATCACTAAACGATAGCACAA	102	2674
1040937	N/A	N/A	172695	172714	AACTCCTTTTAAATTGAATT	111	2675
1040969	N/A	N/A	193065	193084	GGGATTAAATAATTATGTGC	13	2676
1041001	N/A	N/A	209950	209969	GCTAGCATATTTTAAAGAAG	138	2677
1041033	N/A	N/A	233976	233995	CCAGCATTTCAAAGAGCAAC	69	2678
1041065	N/A	N/A	256246	256265	GGCATGTTTATATAACAGCC	124	2679
1041097	N/A	N/A	273626	273645	TTCCTAAAAGAATTTATCCA	108	2680
1041129	N/A	N/A	291710	291729	GTTTCAATATTTTATGCAAA	3	2681
1041161	N/A	N/A	322739	322758	GCAGTAATAATTTAGCCAAA	5	2682
1041193	N/A	N/A	343540	343559	GCTATTAGACAATATAGAGT	2	2683
1041225	N/A	N/A	369454	369473	CACTTCAAACCTTTATCAGT	30	2684
1041257	N/A	N/A	389567	389586	AATCCTTTAATTTAACAACC	111	2685
1041289	N/A	N/A	423903	423922	CCATGAAGAATTTAACCTCA	90	2686

1041321	N/A	N/A	437795	437814	GGAGGTTAATTCATTACACA	6	2687
1041353	N/A	N/A	438249	438268	TGGCCTTATCATACCTAAAT	80	2688
1041385	N/A	N/A	438553	438572	ATTGATCACCCCAGCACCAG	88	2689
1041417	N/A	N/A	439149	439168	TTACCCCAAGCCCAGCAGGT	95	2690
1041449	N/A	N/A	439514	439533	CCCAAAACAATTCAAACCAT	69	2691
1041481	N/A	N/A	440158	440177	ATTTTCTTTCTCCTAGTACC	69	2692
1041513	N/A	N/A	440406	440425	AGAGGCTGCCAGGCCTGGGA	106	2693
1041545	N/A	N/A	441288	441307	TGGAACCTCAATTAAGTCCA	75	2694
1041577	N/A	N/A	441617	441636	ACCACCATACTATATCACAC	37	2695
1041609	N/A	N/A	442257	442276	CCCTCAGTTTTATATGCCAT	17	2696
1041641	N/A	N/A	442708	442727	ACTTATGGCCTCAAACTTGG	63	2697
1041673	N/A	N/A	443057	443076	AAGTTCAGCCTTCTTTCTAG	28	2698
1041705	N/A	N/A	443498	443517	AGCACTTTACCAATACATTT	46	2699
1041737	N/A	N/A	443961	443980	ACTATCTATTTTTTGATACA	63	2700
1041769	N/A	N/A	444350	444369	GTAACCAATCTATCACACCA	20	2701
1041801	N/A	N/A	445255	445274	ATCCCACATTAAAAGCTGGG	121	2702
1041833	N/A	N/A	445608	445627	GCATTCTTAACTTTGTCTGC	47	2703
1041865	N/A	N/A	445874	445893	GTGCTATGTCTATATACACA	71	2704
1041897	N/A	N/A	446067	446086	GGGCTCATAATTATTTTTTA	103	2705
1041929	N/A	N/A	446685	446704	GAATAGCCTTTATAACTTTT	12	2706
1041961	N/A	N/A	446928	446947	TCAGTTATTTTCTCTCCACT	9	2707
1041993	N/A	N/A	447709	447728	CCTGCCAAAAAATCTTCTTC	127	2708
1042025	N/A	N/A	448483	448502	TTGCTGGTTCTTTAACCCCT	31	2709
1042057	N/A	N/A	448731	448750	CGGCTGTTCAATCAAGCACC	85	2710
1042089	N/A	N/A	449073	449092	CCTCAAAATATTATTGAGGG	153	2711
1042121	N/A	N/A	449627	449646	TGAAGAAATCTCACTGAGGG	149	2712
1042153	N/A	N/A	449929	449948	AGATTATTCAGATAATCTGA	125	2713
1042185	N/A	N/A	450548	450567	CCTTAGAATTAAATGCTGTG	84	2714
1042217	N/A	N/A	451193	451212	TCCTCGATACTAACCCCTTC	93	2715
1042249	N/A	N/A	451674	451693	TCAAAACTCCAAAGACACCA	67	2716
1042281	N/A	N/A	451935	451954	GAGCCACATTATACACACTT	30	2717
1042313	N/A	N/A	452254	452273	CCTCTTAGAGTCATTAACAA	62	2718
1042345	N/A	N/A	452531	452550	AGTAGGATCCAAAGGCATGA	29	2719
1042377	N/A	N/A	453048	453067	GTTCTGATACATTTCTAGAA	37	2720
1042409	N/A	N/A	453856	453875	GAACTCACAGTTTACATCTC	53	2721
1042441	N/A	N/A	454688	454707	TGTAGAATTAAAATATACAC	95	2722
1042473	N/A	N/A	455314	455333	TGAGTCCCTAAAACTGGATT	112	2723
1042505	N/A	N/A	456275	456294	TCCTTTCTAGATGTAGTAGA	25	2724
1042537	N/A	N/A	456984	457003	GTTTGCAAACCTCCCTCTCC	101	2725

Table 37

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040106	2686	2705	437405	437424	GGAGCCTTTCATGAAGTAGG	28	2726
1040138	3195	3214	457448	457467	TCTGGAAACTTCAGTTCGCC	91	2727
1040170	3984	4003	458237	458256	TTAACTTTCCAAATCTGCCA	21	2728
1040202	4491	4510	458744	458763	CTTCAAAATCTAATTCCTCA	43	2729
1040234	4745	4764	458998	459017	TACTAGTTCATAATTCACAT	29	2730
1040266	5164	5183	459417	459436	TCTCAGAGTTTCTAAGAGCC	28	2731
1040298	5494	5513	459747	459766	ATTTGTTCAGTTTAGTTGCA	10	2732
1040330	5934	5953	460187	460206	GAGAACAAAGTCTATGTGGC	19	2733
1040362	6304	6323	460557	460576	GGCTCCTTCCCTCCAGCCCT	115	2734
1040394	7078	7097	461331	461350	TTGGTTTCTTATTAATAGTA	11	2735
1040426	7579	7598	461832	461851	TTGTACAACCCTACTCCAGA	78	2736
1040458	7985	8004	462238	462257	GGTTCATGAAACAGTAGCCA	93	2737
1040490	8319	8338	462572	462591	TATGCCAGAAACACAACACT	86	2738
1040522	8669	8688	462922	462941	ACATGTAACTTTCAACCCTT	29	2739
1040554	9051	9070	463304	463323	TTTTTGTCCCCATAATGAGT	34	2740
1040586	9396	9415	463649	463668	GGGACATGAAAAACTGAAGC	22	2741
1040618	9830	9849	464083	464102	AGGATTTACCCCACTCCTGG	82	2742
1040650	10228	10247	464481	464500	ATTTTCTTTTCAATAAGGTG	17	2743
1040682	10481	10500	464734	464753	TCTACCTAGAAAACCTGCAA	44	2744
1040714	N/A	N/A	14865	14884	CTCACATTTTAAAGAGTCTG	41	2745
1040746	N/A	N/A	29049	29068	TCACTGAACCCTTATTTTTT	30	2746
1040778	N/A	N/A	46649	46668	ACTAGAAAAGCCACCCTTCT	129	2747
1040810	N/A	N/A	76238	76257	AGTCTGTATATTTATATTTA	47	2748
1040842	N/A	N/A	92036	92055	CCTTTGTTTTAAAATAGGTA	122	2749
1040874	N/A	N/A	114410	114429	AATGCCAAAGATATACGCCA	6	2750
1040906	N/A	N/A	145082	145101	AGTTAATATCCTTAATACAA	44	2751
1040938	N/A	N/A	173470	173489	AAGTACTATCATTATTGCAT	113	2752
1040970	N/A	N/A	193239	193258	TTCCCCTTATTTTATTCATA	63	2753
1041002	N/A	N/A	210713	210732	TTCCTTCTAGATTAAAGACT	62	2754
1041034	N/A	N/A	234265	234284	AACACAATTTAAATTGAGTT	127	2755
1041066	N/A	N/A	256364	256383	CCTAAGTACCCTTAATTTTT	65	2756
1041098	N/A	N/A	273876	273895	TGTCTATTTCAAAGAAGCGA	80	2757
1041130	N/A	N/A	292765	292784	CACACAATTCAAAACTTGAA	93	2758
1041162	N/A	N/A	322761	322780	AGCAGAATCTAAATCGAACA	22	2759
1041194	N/A	N/A	343565	343584	CGTGTTTTTATTTAACAATA	2	2760
1041226	N/A	N/A	369541	369560	ATTTCTTATATTTATGGGCT	3	2761
1041258	N/A	N/A	391393	391412	TATAGTAGTATTTATAGCTC	28	2762
1041290	N/A	N/A	424357	424376	ACCCCATTTCAAAGACAAGG	59	2763

1041322	N/A	N/A	437796	437815	TGGAGGTTAATTCATTACAC	12	2764
1041354	N/A	N/A	438250	438269	TTGGCCTTATCATACCTAAA	34	2765
1041386	N/A	N/A	438574	438593	GTGCCCAGCCCTTCCACCTG	55	2766
1041418	N/A	N/A	439153	439172	GACTTTACCCCAAGCCCAGC	98	2767
1041450	N/A	N/A	439516	439535	TGCCCAAAACAATTCAAACC	94	2768
1041482	N/A	N/A	440163	440182	AGTTCATTTTCTTTCTCCTA	5	2769
1041514	N/A	N/A	440419	440438	GTCTGGTTTCTGCAGAGGCT	42	2770
1041546	N/A	N/A	441292	441311	CCTTTGGAACCTCAATTAAG	89	2771
1041578	N/A	N/A	441621	441640	TGTCACCACCATACTATATC	26	2772
1041610	N/A	N/A	442258	442277	CCCCTCAGTTTTATATGCCA	45	2773
1041642	N/A	N/A	442717	442736	GCGCCACAGACTTATGGCCT	142	2774
1041674	N/A	N/A	443092	443111	GGCAGGGTAAAAATGGCTTA	52	2775
1041706	N/A	N/A	443499	443518	GAGCACTTTACCAATACATT	23	2776
1041738	N/A	N/A	443965	443984	ACCAACTATCTATTTTTTGA	51	2777
1041770	N/A	N/A	444351	444370	TGTAACCAATCTATCACACC	30	2778
1041802	N/A	N/A	445261	445280	ACACAAATCCCACATTAAAA	92	2779
1041834	N/A	N/A	445611	445630	TGGGCATTCTTAACTTTGTC	28	2780
1041866	N/A	N/A	445897	445916	TTGTATATTTCAATCTTAGA	26	2781
1041898	N/A	N/A	446071	446090	TTCTGGGCTCATAATTATTT	52	2782
1041930	N/A	N/A	446687	446706	TAGAATAGCCTTTATAACTT	33	2783
1041962	N/A	N/A	446929	446948	TTCAGTTATTTTCTCTCCAC	16	2784
1041994	N/A	N/A	447710	447729	TCCTGCCAAAAAATCTTCTT	118	2785
1042026	N/A	N/A	448513	448532	ACTCCCTACACTGTAGCAAC	97	2786
1042058	N/A	N/A	448749	448768	AATGGTATCCCATTCTTCCG	63	2787
1042090	N/A	N/A	449075	449094	GGCCTCAAAATATTATTGAG	107	2788
1042122	N/A	N/A	449649	449668	TTAACTGATCATTAACCGTT	49	2789
1042154	N/A	N/A	449930	449949	AAGATTATTCAGATAATCTG	178	2790
1042186	N/A	N/A	450550	450569	GGCCTTAGAATTAAATGCTG	145	2791
1042218	N/A	N/A	451194	451213	CTCCTCGATACTAACCCCTT	118	2792
1042250	N/A	N/A	451676	451695	TCTCAAAACTCCAAAGACAC	80	2793
1042282	N/A	N/A	451937	451956	GTGAGCCACATTATACACAC	69	2794
1042314	N/A	N/A	452263	452282	TCTTGCAAACCTCTTAGAGT	74	2795
1042346	N/A	N/A	452544	452563	ATTGACTGAAATAAGTAGGA	16	2796
1042378	N/A	N/A	453050	453069	TAGTTCTGATACATTTCTAG	47	2797
1042410	N/A	N/A	453883	453902	CATATTATCTCCAAATAAGC	124	2798
1042442	N/A	N/A	454701	454720	GGTCTATGAGAATTGTAGAA	32	2799
1042474	N/A	N/A	455315	455334	CTGAGTCCCTAAAACTGGAT	78	2800
1042506	N/A	N/A	456290	456309	AGTCAATTTCCAATGTCCTT	21	2801
1042538	N/A	N/A	456985	457004	AGTTTGCAAACCTCCCTCTC	117	2802

Table 38

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040107	2687	2706	437406	437425	TGGAGCCTTTCATGAAGTAG	23	2803
1040139	3196	3215	457449	457468	CTCTGGAAACTTCAGTTCGC	87	2804
1040171	3985	4004	458238	458257	GTTAACTTTCCAAATCTGCC	23	2805
1040203	4493	4512	458746	458765	ATCTTCAAAATCTAATTCCT	45	2806
1040235	4746	4765	458999	459018	ATACTAGTTCATAATTCACA	35	2807
1040267	5172	5191	459425	459444	AAGAAAATTCTCAGAGTTTC	56	2808
1040299	5502	5521	459755	459774	AGTCAGGTATTTGTTCAGTT	5	2809
1040331	5952	5971	460205	460224	GTAAATAGTGATATTAATGA	53	2810
1040363	6365	6384	460618	460637	GCTCCCCGCCCCAGCACTCA	102	2811
1040395	7081	7100	461334	461353	TTGTTGGTTTCTTATTAATA	16	2812
1040427	7580	7599	461833	461852	ATTGTACAACCCTACTCCAG	70	2813
1040459	7987	8006	462240	462259	GTGGTTCATGAAACAGTAGC	88	2814
1040491	8321	8340	462574	462593	CCTATGCCAGAAACACAACA	72	2815
1040523	8683	8702	462936	462955	CTATATACAAAAAAACATGT	121	2816
1040555	9099	9118	463352	463371	CCCCCATTTAAATGAGGTGT	141	2817
1040587	9424	9443	463677	463696	CAGTTGAACCATTTGTATGC	22	2818
1040619	9842	9861	464095	464114	TGCACTAACTAAAGGATTTA	46	2819
1040651	10229	10248	464482	464501	AATTTTCTTTTCAATAAGGT	93	2820
1040683	10482	10501	464735	464754	TTCTACCTAGAAAACCTGCA	41	2821
1040715	N/A	N/A	16686	16705	CTCGAAAAACATATCCCCCA	52	2822
1040747	N/A	N/A	29088	29107	TGGTAATTTTAAAATATGGG	15	2823
1040779	N/A	N/A	48578	48597	GTGTTAATTCAAAAAATTTC	119	2824
1040811	N/A	N/A	76251	76270	TGCATACAAATTTAGTCTGT	21	2825
1040843	N/A	N/A	93032	93051	TCTAGATTACAAACCATCCT	110	2826
1040875	N/A	N/A	114768	114787	TTTCATTTTATTTAAGCCAA	20	2827
1040907	N/A	N/A	146636	146655	AAGATGTTTTAAAATCTGAC	107	2828
1040939	N/A	N/A	174742	174761	GTACTTGTTCCTTAACCAAG	149	2829
1040971	N/A	N/A	193345	193364	TCAGTTTACCTTTAATGGAA	30	2830
1041003	N/A	N/A	211774	211793	TGCTCAATATTTTAAACATT	44	2831
1041035	N/A	N/A	234289	234308	GTCGGATAAATTTATCCACA	131	2832
1041067	N/A	N/A	256544	256563	TTAGCAAACATTTATGAGCA	45	2833
1041099	N/A	N/A	274538	274557	CTTCCAATCCATTACATCTT	81	2834
1041131	N/A	N/A	293124	293143	CCTTCCAACCCTTAGCCTTT	12	2835
1041163	N/A	N/A	323168	323187	AGCCAAAAACCCATGGACCA	120	2836
1041195	N/A	N/A	343967	343986	ACAGTAATCTTTTATACAAG	19	2837
1041227	N/A	N/A	369669	369688	TTCCCGAACCCTTAAGGATA	99	2838
1041259	N/A	N/A	391405	391424	AGTTGACACCTTTATAGTAG	4	2839
1041291	N/A	N/A	424646	424665	GTCTTAAAACTATTCACTGT	81	2840

1041323	N/A	N/A	437820	437839	ATAACTAGCCCCACTCTCCA	98	2841
1041355	N/A	N/A	438251	438270	GTTGGCCTTATCATACCTAA	21	2842
1041387	N/A	N/A	438878	438897	GCTGCCTTCCATCTGTTTTT	90	2843
1041419	N/A	N/A	439154	439173	TGACTTTACCCCAAGCCCAG	109	2844
1041451	N/A	N/A	439554	439573	GAGACAAGAAACACTGTCTC	153	2845
1041483	N/A	N/A	440171	440190	CTCAAGGTAGTTCATTTTCT	10	2846
1041515	N/A	N/A	440723	440742	GCCTACAATCCCAGCTTTAG	88	2847
1041547	N/A	N/A	441337	441356	GAGAAAACCCCTCAGGAAGG	115	2848
1041579	N/A	N/A	441623	441642	TCTGTCACCACCATACTATA	57	2849
1041611	N/A	N/A	442265	442284	CTAAACACCCCTCAGTTTTA	100	2850
1041643	N/A	N/A	442722	442741	TGGATGCGCCACAGACTTAT	59	2851
1041675	N/A	N/A	443093	443112	AGGCAGGGTAAAAATGGCTT	66	2852
1041707	N/A	N/A	443502	443521	CCAGAGCACTTTACCAATAC	30	2853
1041739	N/A	N/A	443966	443985	CACCAACTATCTATTTTTTG	47	2854
1041771	N/A	N/A	444355	444374	CAGTTGTAACCAATCTATCA	22	2855
1041803	N/A	N/A	445267	445286	CTCCTAACACAAATCCCACA	124	2856
1041835	N/A	N/A	445625	445644	CGAAATTATTAAATTGGGCA	36	2857
1041867	N/A	N/A	445899	445918	GATTGTATATTTCAATCTTA	55	2858
1041899	N/A	N/A	446086	446105	ACAACACCGACTCACTTCTG	41	2859
1041931	N/A	N/A	446708	446727	TCAAACACCCTAAGCAGTAA	74	2860
1041963	N/A	N/A	446930	446949	CTTCAGTTATTTTCTCTCCA	10	2861
1041995	N/A	N/A	447711	447730	ATCCTGCCAAAAAATCTTCT	100	2862
1042027	N/A	N/A	448517	448536	CCTTACTCCCTACACTGTAG	99	2863
1042059	N/A	N/A	448770	448789	ATGTTCTTCCCCATCTCCAT	36	2864
1042091	N/A	N/A	449076	449095	CGGCCTCAAAATATTATTGA	165	2865
1042123	N/A	N/A	449669	449688	GATATAAACATTCTTAAAGG	92	2866
1042155	N/A	N/A	449932	449951	GGAAGATTATTCAGATAATC	24	2867
1042187	N/A	N/A	450551	450570	AGGCCTTAGAATTAAATGCT	137	2868
1042219	N/A	N/A	451198	451217	CAGTCTCCTCGATACTAACC	67	2869
1042251	N/A	N/A	451677	451696	ATCTCAAAACTCCAAAGACA	87	2870
1042283	N/A	N/A	451938	451957	TGTGAGCCACATTATACACA	69	2871
1042315	N/A	N/A	452264	452283	CTCTTGCAAACCTCTTAGAG	99	2872
1042347	N/A	N/A	452571	452590	TCCTGCTACCCCCCAACAGT	124	2873
1042379	N/A	N/A	453088	453107	TTCATCTTCTTTGTTTCCTT	25	2874
1042411	N/A	N/A	453892	453911	AACAAAATACATATTATCTC	99	2875
1042443	N/A	N/A	454927	454946	CCGTTTCTACAGAAATTTAA	78	2876
1042475	N/A	N/A	455316	455335	TCTGAGTCCCTAAAACTGGA	90	2877
1042507	N/A	N/A	456620	456639	CCCAGCCCCTAAAAGGATGC	118	2878
1042539	N/A	N/A	457035	457054	AGGTATGAACTCACACAGAC	63	2879

Table 39

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040108	2725	2744	437444	437463	TTCCACCTTCTTTAGCTCCC	67	2880
1040140	3212	3231	457465	457484	CAGGCAATCCCATTTTCTCT	84	2881
1040172	4000	4019	458253	458272	ATGTTCTTTTAAATGGTTAA	15	2882
1040204	4494	4513	458747	458766	CATCTTCAAAATCTAATTCC	66	2883
1040236	4749	4768	459002	459021	CACATACTAGTTCATAATTC	20	2884
1040268	5188	5207	459441	459460	TCTCTCAATGAATCTGAAGA	26	2885
1040300	5514	5533	459767	459786	GGGTAAAAGAAAAGTCAGGT	10	2886
1040332	5954	5973	460207	460226	TTGTAAATAGTGATATTAAT	74	2887
1040364	6439	6458	460692	460711	CTGCGGTTCCTCCCCCGGGT	124	2888
1040396	7117	7136	461370	461389	ATATATTTAGAAATCCCTAG	82	2889
1040428	7581	7600	461834	461853	AATTGTACAACCCTACTCCA	98	2890
1040460	8014	8033	462267	462286	GCAACAGACCAGTCTGTTGA	113	2891
1040492	8323	8342	462576	462595	TCCCTATGCCAGAAACACAA	70	2892
1040524	8684	8703	462937	462956	TCTATATACAAAAAAACATG	103	2893
1040556	9100	9119	463353	463372	CCCCCCATTTAAATGAGGTG	114	2894
1040588	9426	9445	463679	463698	TACAGTTGAACCATTTGTAT	67	2895
1040620	9862	9881	464115	464134	GCACAGGTATCAAGTTCAAA	17	2896
1040652	10235	10254	464488	464507	ACTTAAAATTTTCTTTTCAA	109	2897
1040684	10493	10512	464746	464765	AATGAAATAATTTCTACCTA	55	2898
1040716	N/A	N/A	16822	16841	GGCACATTTTAAAAAGAAGC	23	2899
1040748	N/A	N/A	30745	30764	TGTTTGCTATTTTAAGAGCC	24	2900
1040780	N/A	N/A	48620	48639	GCTAGTAAAATTTAGGGCAG	36	2901
1040812	N/A	N/A	76786	76805	TCTGAAAAACCTCTTCCTCT	60	2902
1040844	N/A	N/A	93297	93316	GATGCATTTCATTACTGCTT	41	2903
1040876	N/A	N/A	114844	114863	ATGTAATATTAAATAGCATC	70	2904
1040908	N/A	N/A	148861	148880	AGGTAATTTCAAAGCTTCCA	4	2905
			149972	149991			
1040940	N/A	N/A	175616	175635	CTTTCAATTCCTTAAAAGGA	101	2906
1040972	N/A	N/A	195063	195082	ACACACAAAGAATGAACCAT	57	2907
1041004	N/A	N/A	212966	212985	ATCCTAATTCAAAAACTAGT	131	2908
1041036	N/A	N/A	235568	235587	AGCCATAAAACCATGCGGTT	91	2909
1041068	N/A	N/A	256941	256960	TTACCCAAATTATCACTGTA	47	2910
1041100	N/A	N/A	274711	274730	GGACTTAACCCTTACTCCAA	84	2911
1041132	N/A	N/A	293412	293431	TGTTAGCTATTTTATATGGA	2	2912
1041164	N/A	N/A	323174	323193	TTACACAGCCAAAAACCCAT	100	2913
1041196	N/A	N/A	344505	344524	TGAGTAATTTAAAATGCCCA	43	2914
1041228	N/A	N/A	369876	369895	AAGGTCTGCCTTTAACATTT	14	2915
1041260	N/A	N/A	392003	392022	GTAAAATTTCTTTATGTGTG	4	2916

1041292	N/A	N/A	424647	424666	AGTCTTAAAACTATTCACTG	78	2917
1041324	N/A	N/A	437831	437850	TCAAGGACTCCATAACTAGC	111	2918
1041356	N/A	N/A	438263	438282	GCTGATCTATCTGTTGGCCT	58	2919
1041388	N/A	N/A	438882	438901	TAGGGCTGCCTTCCATCTGT	51	2920
1041420	N/A	N/A	439156	439175	GCTGACTTTACCCCAAGCCC	100	2921
1041452	N/A	N/A	439834	439853	AATGCTCAAAAAAGCCAGAC	54	2922
1041484	N/A	N/A	440190	440209	CTGTGAAGAGTCAACTTTGC	65	2923
1041516	N/A	N/A	440724	440743	CGCCTACAATCCCAGCTTTA	93	2924
1041548	N/A	N/A	441358	441377	GGAAGATTCTTCAGGCTAGG	11	2925
1041580	N/A	N/A	441624	441643	GTCTGTCACCACCATACTAT	34	2926
1041612	N/A	N/A	442271	442290	CCCAAACTAAACACCCCTCA	97	2927
1041644	N/A	N/A	442787	442806	AGCCCCATCCTTCTTTTGAG	88	2928
1041676	N/A	N/A	443103	443122	CGAGGATTACAGGCAGGGTA	15	2929
1041708	N/A	N/A	443511	443530	CGTGTCAACCCAGAGCACTT	120	2930
1041740	N/A	N/A	443969	443988	AGTCACCAACTATCTATTTT	53	2931
1041772	N/A	N/A	444356	444375	TCAGTTGTAACCAATCTATC	20	2932
1041804	N/A	N/A	445269	445288	GCCTCCTAACACAAATCCCA	93	2933
1041836	N/A	N/A	445626	445645	GCGAAATTATTAAATTGGGC	50	2934
1041868	N/A	N/A	445900	445919	TGATTGTATATTTCAATCTT	114	2935
1041900	N/A	N/A	446090	446109	GGAGACAACACCGACTCACT	81	2936
1041932	N/A	N/A	446710	446729	TTTCAAACACCCTAAGCAGT	92	2937
1041964	N/A	N/A	446938	446957	GAATCACACTTCAGTTATTT	19	2938
1041996	N/A	N/A	447713	447732	CCATCCTGCCAAAAAATCTT	111	2939
1042028	N/A	N/A	448519	448538	CCCCTTACTCCCTACACTGT	95	2940
1042060	N/A	N/A	448773	448792	CCCATGTTCTTCCCCATCTC	70	2941
1042092	N/A	N/A	449077	449096	CCGGCCTCAAAATATTATTG	114	2942
1042124	N/A	N/A	449672	449691	AAGGATATAAACATTCTTAA	73	2943
1042156	N/A	N/A	449935	449954	AGCGGAAGATTATTCAGATA	18	2944
1042188	N/A	N/A	450567	450586	CCAAATCTCCAAAGACAGGC	54	2945
1042220	N/A	N/A	451224	451243	ACTGGTGCCCAAATGTCTAT	54	2946
1042252	N/A	N/A	451679	451698	GCATCTCAAAACTCCAAAGA	31	2947
1042284	N/A	N/A	451940	451959	TGTGTGAGCCACATTATACA	86	2948
1042316	N/A	N/A	452275	452294	CTCCATAGATCCTCTTGCAA	106	2949
1042348	N/A	N/A	452589	452608	AAGAGATGAACTAAGCATTC	52	2950
1042380	N/A	N/A	453101	453120	GTTGCTTTTCTACTTCATCT	21	2951
1042412	N/A	N/A	453897	453916	TCTAGAACAAAATACATATT	131	2952
1042444	N/A	N/A	455045	455064	ATCCATGAAGCCAGGCATGG	165	2953
1042476	N/A	N/A	455318	455337	CATCTGAGTCCCTAAAACTG	93	2954
1042508	N/A	N/A	456623	456642	GTCCCCAGCCCCTAAAAGGA	101	2955
1042540	N/A	N/A	457036	457055	CAGGTATGAACTCACACAGA	56	2956

Table 40

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
1040109	2741	2760	437460	437479	CTTCTGTTTTTAAGTCTTCC	30	2957
1040141	3213	3232	457466	457485	GCAGGCAATCCCATTTTCTC	78	2958
1040173	4010	4029	458263	458282	GGAGAGAAAAATGTTCTTTT	5	2959
1040205	4497	4516	458750	458769	GCTCATCTTCAAAATCTAAT	9	2960
1040237	4758	4777	459011	459030	ATTTATTGTCACATACTAGT	76	2961
1040269	5216	5235	459469	459488	CACATATATAAATGTCTTTA	28	2962
1040301	5533	5552	459786	459805	GAAAGTACTATTTTCAATGG	27	2963
1040333	5959	5978	460212	460231	ATGAGTTGTAAATAGTGATA	22	2964
1040365	6440	6459	460693	460712	ACTGCGGTTCCTCCCCCGGG	111	2965
1040397	7126	7145	461379	461398	AGTCATTTTATATATTTAGA	58	2966
1040429	7601	7620	461854	461873	GAAATCCAAACATTCCTTGA	51	2967
1040461	8061	8080	462314	462333	GCCCTGTTTTCACCTGGTGC	57	2968
1040493	8325	8344	462578	462597	TTTCCCTATGCCAGAAACAC	63	2969
1040525	8685	8704	462938	462957	TTCTATATACAAAAAAACAT	107	2970
1040557	9101	9120	463354	463373	TCCCCCCATTTAAATGAGGT	145	2971
1040589	9439	9458	463692	463711	CACTTAATTTTAATACAGTT	44	2972
1040621	9883	9902	464136	464155	GCAGTATTCACAGAACTGAA	61	2973
1040653	10237	10256	464490	464509	GCACTTAAAATTTTCTTTTC	17	2974
1040685	10507	10526	464760	464779	TGTTTTATTATAATAATGAA	157	2975
1040717	N/A	N/A	17529	17548	ACATCAAAACGATTTCTACT	25	2976
1040749	N/A	N/A	31007	31026	AACCAAAACCAAAAGCCTCT	51	2977
1040781	N/A	N/A	48839	48858	AATCTAAAATACATCTGCAT	103	2978
1040813	N/A	N/A	77220	77239	CAGTTTATTTAAAGATATAA	119	2979
1040845	N/A	N/A	94390	94409	ATCAGTAAAGAATTGATGTC	115	2980
1040877	N/A	N/A	114917	114936	CTTCATAAAATTCCATTCTG	26	2981
1040909	N/A	N/A	148914	148933	GCTTTCATAATATAACAACC	6	2982
			150025	150044			
1040941	N/A	N/A	176494	176513	ATCAACAAAATTATGTATGG	124	2983
1040973	N/A	N/A	195332	195351	GGAAACAACCAAAGTTTTTT	58	2984
1041005	N/A	N/A	213451	213470	CTGTAGTTTTAAAAGTGCCT	15	2985
1041037	N/A	N/A	236934	236953	ACCATATTTCTTTAGAAGGT	70	2986
1041069	N/A	N/A	257007	257026	GTGACCAAAATACATATACT	47	2987
1041101	N/A	N/A	274862	274881	ACTGGATTTATTTAAGTCTT	96	2988
1041133	N/A	N/A	294752	294771	GAGTCTTGCCCTTAAGAAGC	4	2989
1041165	N/A	N/A	323691	323710	TTGATATTTCAAAAGAGCTA	45	2990
1041197	N/A	N/A	344706	344725	ATGTAAATATTTTAGCACAG	3	2991
1041229	N/A	N/A	370271	370290	GACTAATTTTAAAATATGCT	36	2992

1041261	N/A	N/A	392692	392711	GAGATAAAAATTATGTAGTT	86	2993
1041293	N/A	N/A	425116	425135	TGGGATAATATTTATAAGTG	43	2994
1041325	N/A	N/A	437884	437903	ATCTTAATCACAGAATTCAA	46	2995
1041357	N/A	N/A	438268	438287	TGTCTGCTGATCTATCTGTT	14	2996
1041389	N/A	N/A	438883	438902	TTAGGGCTGCCTTCCATCTG	58	2997
1041421	N/A	N/A	439158	439177	CAGCTGACTTTACCCCAAGC	77	2998
1041453	N/A	N/A	439844	439863	GCATTTAAGAAATGCTCAAA	132	2999
1041485	N/A	N/A	440217	440236	GTTTATTTTCCATGTGTCAC	2	3000
1041517	N/A	N/A	440772	440791	CTCCCCAAGAACAGAAGAGG	149	3001
1041549	N/A	N/A	441359	441378	AGGAAGATTCTTCAGGCTAG	17	3002
1041581	N/A	N/A	441646	441665	AGACCCAAATCCGCACCCCT	134	3003
1041613	N/A	N/A	442273	442292	TCCCCAAACTAAACACCCCT	106	3004
1041645	N/A	N/A	442814	442833	TACTTCCTACCCAAGGAGGA	124	3005
1041677	N/A	N/A	443114	443133	GGATTCCACCCCGAGGATTA	120	3006
1041709	N/A	N/A	443555	443574	CCCTAATAACACAGAGCCTG	113	3007
1041741	N/A	N/A	443971	443990	GCAGTCACCAACTATCTATT	47	3008
1041773	N/A	N/A	444357	444376	ATCAGTTGTAACCAATCTAT	16	3009
1041805	N/A	N/A	445298	445317	TCAGTAAACCCACACCCTAG	109	3010
1041837	N/A	N/A	445627	445646	GGCGAAATTATTAAATTGGG	100	3011
1041869	N/A	N/A	445902	445921	TTTGATTGTATATTTCAATC	85	3012
1041901	N/A	N/A	446109	446128	GATGGACGAACCTAGACAGG	54	3013
1041933	N/A	N/A	446716	446735	ATCCTGTTTCAAACACCCTA	27	3014
1041965	N/A	N/A	446945	446964	TTTTATTGAATCACACTTCA	41	3015
1041997	N/A	N/A	447722	447741	TCCCTCTTCCCATCCTGCCA	89	3016
1042029	N/A	N/A	448526	448545	GCATGTGCCCCTTACTCCCT	84	3017
1042061	N/A	N/A	448774	448793	TCCCATGTTCTTCCCCATCT	72	3018
1042093	N/A	N/A	449386	449405	AGCTTCAAAATATTGTTATT	53	3019
1042125	N/A	N/A	449674	449693	ATAAGGATATAAACATTCTT	59	3020
1042157	N/A	N/A	449937	449956	GGAGCGGAAGATTATTCAGA	33	3021
1042189	N/A	N/A	450569	450588	CTCCAAATCTCCAAAGACAG	86	3022
1042221	N/A	N/A	451237	451256	TTCTTGAACCCTCACTGGTG	100	3023
1042253	N/A	N/A	451681	451700	CCGCATCTCAAAACTCCAAA	9	3024
1042285	N/A	N/A	451942	451961	GGTGTGTGAGCCACATTATA	47	3025
1042317	N/A	N/A	452277	452296	GGCTCCATAGATCCTCTTGC	95	3026
1042349	N/A	N/A	452631	452650	TGACCTCTACCCTTGTGAGC	47	3027
1042381	N/A	N/A	453102	453121	TGTTGCTTTTCTACTTCATC	73	3028
1042413	N/A	N/A	453898	453917	CTCTAGAACAAAATACATAT	88	3029
1042445	N/A	N/A	455059	455078	TCTGTTTTTAAAAGATCCAT	36	3030
1042477	N/A	N/A	455353	455372	AACAGGCCTTTCAAGGTCTG	123	3031
1042509	N/A	N/A	456640	456659	AGTGTGTTTATCACTGAGTC	97	3032
1042541	N/A	N/A	457060	457079	CTTGTTTGATTTTATGCACA	92	3033

Table 41

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
1040110	2743	2762	437462	437481	ATCTTCTGTTTTTAAGTCTT	41	3034
1040142	3214	3233	457467	457486	TGCAGGCAATCCCATTTTCT	99	3035
1040174	4012	4031	458265	458284	TTGGAGAGAAAAATGTTCTT	23	3036
1040206	4499	4518	458752	458771	ATGCTCATCTTCAAAATCTA	23	3037
1040238	4763	4782	459016	459035	TGGTCATTTATTGTCACATA	6	3038
1040270	5220	5239	459473	459492	TGCTCACATATATAAATGTC	36	3039
1040302	5570	5589	459823	459842	GTTGATACCAGATTTTTTTT	30	3040
1040334	6015	6034	460268	460287	AGTCAATTCAATACTCGAAG	6	3041
1040366	6474	6493	460727	460746	TCCACATTCACTATTCCGTG	17	3042
1040398	7128	7147	461381	461400	ACAGTCATTTTATATATTTA	34	3043
1040430	7604	7623	461857	461876	CAGGAAATCCAAACATTCCT	130	3044
1040462	8106	8125	462359	462378	TCACATCACCACCGAAGAAA	40	3045
1040494	8331	8350	462584	462603	TTGGAGTTTCCCTATGCCAG	17	3046
1040526	8692	8711	462945	462964	GACAAATTTCTATATACAAA	57	3047
1040558	9103	9122	463356	463375	ACTCCCCCCATTTAAATGAG	116	3048
1040590	9440	9459	463693	463712	GCACTTAATTTTAATACAGT	15	3049
1040622	9884	9903	464137	464156	GGCAGTATTCACAGAACTGA	41	3050
1040654	10253	10272	464506	464525	CTTAACTATTATGTATGCAC	17	3051
1040686	10508	10527	464761	464780	TTGTTTTATTATAATAATGA	195	3052
1040718	N/A	N/A	17546	17565	GCAGGTAAAACCAAATGACA	121	3053
1040750	N/A	N/A	31009	31028	GCAACCAAAACCAAAAGCCT	67	3054
1040782	N/A	N/A	49205	49224	GGGCTATTAATTTATTAAAT	123	3055
1040814	N/A	N/A	77279	77298	AAGATCTTTTAAAGTCCTAC	58	3056
1040846	N/A	N/A	94692	94711	GTAAGCTCCATTTATAGAAT	30	3057
1040878	N/A	N/A	117437	117456	CCTCACACACCTTAACCCTG	95	3058
1040910	N/A	N/A	151015	151034	GAGATAAAAATTATTTTGGC	108	3059
1040942	N/A	N/A	176706	176725	GCTAAATTTCATTAGAAACA	115	3060
1040974	N/A	N/A	195854	195873	TTTTCTACAATTTATAGGCG	27	3061
1041006	N/A	N/A	215585	215604	CTGCACCAAATTTATTTTTG	37	3062
1041038	N/A	N/A	237026	237045	ACTGAAAAAACTGTATGATC	99	3063
1041070	N/A	N/A	257572	257591	CCTTTTAAAATTTCCAGAAA	97	3064
1041102	N/A	N/A	276104	276123	GAAGTTAGCCAGGCATCAGG	77	3065
1041134	N/A	N/A	294914	294933	GCAGAGTTTTAAAATGCACT	14	3066
1041166	N/A	N/A	324245	324264	AGGCATAGTATTTAGCAGAA	2	3067
1041198	N/A	N/A	345616	345635	TACTTCTTTCCTTAAGCACA	6	3068
1041230	N/A	N/A	370434	370453	TAGTTTAAAATATGTGACTC	96	3069
1041262	N/A	N/A	393162	393181	CCAGAAAAACCTTAAACTAC	73	3070
1041294	N/A	N/A	425225	425244	ACCTTCAAACTATCAATTCT	105	3071

1041326	N/A	N/A	437890	437909	TTCCTCATCTTAATCACAGA	25	3072
1041358	N/A	N/A	438300	438319	GAGAGTATAAAAATTATCTC	102	3073
1041390	N/A	N/A	438894	438913	GTCCATCACACTTAGGGCTG	37	3074
1041422	N/A	N/A	439161	439180	CTACAGCTGACTTTACCCCA	50	3075
1041454	N/A	N/A	439848	439867	TTGGGCATTTAAGAAATGCT	116	3076
1041486	N/A	N/A	440219	440238	ATGTTTATTTTCCATGTGTC	3	3077
1041518	N/A	N/A	440776	440795	CTTCCTCCCCAAGAACAGAA	88	3078
1041550	N/A	N/A	441384	441403	CAGTGCCTAACCAGTTGAGA	28	3079
1041582	N/A	N/A	441650	441669	CCAGAGACCCAAATCCGCAC	65	3080
1041614	N/A	N/A	442275	442294	CATCCCCAAACTAAACACCC	95	3081
1041646	N/A	N/A	442820	442839	CTAACCTACTTCCTACCCAA	133	3082
1041678	N/A	N/A	443164	443183	AGCCTTAGAAACAGGAACGG	46	3083
1041710	N/A	N/A	443556	443575	GCCCTAATAACACAGAGCCT	142	3084
1041742	N/A	N/A	444005	444024	CGGCACAAATCCAGGGCTGG	87	3085
1041774	N/A	N/A	444387	444406	TAGTTAAAAATAAGGTATCG	87	3086
1041806	N/A	N/A	445299	445318	TTCAGTAAACCCACACCCTA	110	3087
1041838	N/A	N/A	445628	445647	TGGCGAAATTATTAAATTGG	102	3088
1041870	N/A	N/A	445919	445938	CACGCATATTTATGCTGTTT	86	3089
1041902	N/A	N/A	446110	446129	GGATGGACGAACCTAGACAG	34	3090
1041934	N/A	N/A	446718	446737	ATATCCTGTTTCAAACACCC	43	3091
1041966	N/A	N/A	446947	446966	GATTTTATTGAATCACACTT	19	3092
1041998	N/A	N/A	447903	447922	CAACCATTCCAGACTGAGCT	109	3093
1042030	N/A	N/A	448548	448567	ACATGCAAGCCTGATGTGGT	121	3094
1042062	N/A	N/A	448818	448837	CTAAAACACACCAGACCTCC	91	3095
1042094	N/A	N/A	449387	449406	TAGCTTCAAAATATTGTTAT	62	3096
1042126	N/A	N/A	449684	449703	TAGGTTTGTCATAAGGATAT	11	3097
1042158	N/A	N/A	449978	449997	GCCACGACCAGATATCAGCT	39	3098
1042190	N/A	N/A	450570	450589	ACTCCAAATCTCCAAAGACA	95	3099
1042222	N/A	N/A	451238	451257	CTTCTTGAACCCTCACTGGT	119	3100
1042254	N/A	N/A	451682	451701	TCCGCATCTCAAAACTCCAA	28	3101
1042286	N/A	N/A	451968	451987	GGACACCTACCCATGGAGAG	57	3102
1042318	N/A	N/A	452311	452330	ACTGTATTCTAAGTAGGAGG	23	3103
1042350	N/A	N/A	452636	452655	CCTCCTGACCTCTACCCTTG	77	3104
1042382	N/A	N/A	453115	453134	GATTTCCACAGATTGTTGCT	66	3105
1042414	N/A	N/A	453899	453918	CCTCTAGAACAAAATACATA	36	3106
1042446	N/A	N/A	455060	455079	ATCTGTTTTTAAAAGATCCA	71	3107
1042478	N/A	N/A	455364	455383	AACCACAAGCCAACAGGCCT	114	3108
1042510	N/A	N/A	456663	456682	TGTGAGTTCCAAGAAGCAGG	54	3109
1042542	N/A	N/A	457069	457088	CATTTTATTCTTGTTTGATT	149	3110

Table 42

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
994630	N/A	N/A	85516	85535	GTTTGATATGCTATGCTCAC	12	219
994693	N/A	N/A	184184	184203	TCAGGTTTATATGTATACAA	2	149
994706	N/A	N/A	217284	217303	GTTATGTTTAAGGTATTTTC	5	540
994735	N/A	N/A	297005	297024	GTTTGCATTAAATGACTGTG	1	310
1054946	101	120	2611	2630	CTGTTGCTCTGGCTGCTGCT	10	3111
1054950	110	129	2620	2639	TTGCGGCTGCTGTTGCTCTG	14	3112
1054955	117	136	2627	2646	CAATGTCTTGCGGCTGCTGT	24	3113
1054966	248	267	10659	10678	CCTGGTGACTTGATGCACGA	25	3114
1054972	552	571	178162	178181	ATCAGTTCCTTGCAGCAGAT	3	3115
1054978	561	580	178171	178190	CCATAAGCTATCAGTTCCTT	2	3116
1054983	568	587	178178	178197	TGGAGAACCATAAGCTATCA	8	3117
1054989	586	605	178196	178215	CATGTGCTTTCATCACAATG	63	3118
1054994	592	611	178202	178221	CTGTACCATGTGCTTTCATC	2	3119
1055000	3487	3506	457740	457759	TAAATACTGTGTTATTTTAG	72	3120
1055004	5497	5516	459750	459769	GGTATTTGTTCAGTTTAGTT	6	3121
1055008	5503	5522	459756	459775	AAGTCAGGTATTTGTTCAGT	5	3122
1055014	6028	6047	460281	460300	GTTTAGTGGATCCAGTCAAT	16	3123
1055018	6035	6054	460288	460307	AGTGTTGGTTTAGTGGATCC	32	3124
1055023	6044	6063	460297	460316	TCCCATCTTAGTGTTGGTTT	28	3125
1055029	9484	9503	463737	463756	TTAGAGATTGTTGTTATTGT	13	3126
1055034	9490	9509	463743	463762	AAATTCTTAGAGATTGTTGT	14	3127
1055039	10090	10109	464343	464362	TGATCTGATATTAAAACATC	78	3128
1055044	10097	10116	464350	464369	TGGGTAATGATCTGATATTA	13	3129
1055050	10106	10125	464359	464378	GGCATATGGTGGGTAATGAT	12	3130
1055056	196	215	9912	9931	AGTAGTTTTTGTGAGGTAAA	11	3131
1055060	202	221	9918	9937	GCTTGTAGTAGTTTTTGTGA	29	3132
1055064	N/A	N/A	17720	17739	TTTTCTATTTGCACTAGCTG	65	3133
1055070	N/A	N/A	17728	17747	ATGTCACCTTTTCTATTTGC	3	3134
1055076	N/A	N/A	24689	24708	AAACACTAGAAATCCAGGGA	7	3135
1055082	N/A	N/A	85508	85527	TGCTATGCTCACAGAGAACC	78	3136
1055093	N/A	N/A	85524	85543	TACAGTTAGTTTGATATGCT	25	3137
1055098	N/A	N/A	108194	108213	GGAATAAATTATTTACTGCG	5	3138
1055104	N/A	N/A	148323	148342	TACTATGTATTTGCCACAGT	6	3139
			149434	149453			
1055110	N/A	N/A	179786	179805	ATATTTAATCATGTTCCCGA	13	3140
1055115	N/A	N/A	179792	179811	ATAGTTATATTTAATCATGT	67	3141
1055120	N/A	N/A	184176	184195	ATATGTATACAATTCTGACA	38	3142
1055131	N/A	N/A	184192	184211	CAATGTTCTCAGGTTTATAT	15	3143

1055137	N/A	N/A	203033	203052	CCTTTCTTCTTTGTTCATAG	6	3144
1055142	N/A	N/A	203039	203058	CTTGTTCCTTTCTTCTTTGT	31	3145
1055148	N/A	N/A	203883	203902	ATTTATCCTCAGGATGCAAA	55	3146
1055154	N/A	N/A	203892	203911	TTTGTTTAGATTTATCCTCA	6	3147
1055159	N/A	N/A	210724	210743	ATACTCCATTTTTCCTTCTA	19	3148
1055164	N/A	N/A	210731	210750	ATGTGTAATACTCCATTTTT	25	3149
1055170	N/A	N/A	210740	210759	TTATTACAAATGTGTAATAC	107	3150
1055176	N/A	N/A	212029	212048	TATGTTAGTCATTTCTCTCT	28	3151
1055181	N/A	N/A	212035	212054	CAAGTCTATGTTAGTCATTT	10	3152
1055187	N/A	N/A	217276	217295	TAAGGTATTTTCATGGAGTT	12	3153
1055198	N/A	N/A	217292	217311	TTGTAACAGTTATGTTTAAG	43	3154
1055204	N/A	N/A	226990	227009	TTTACTCATTCTACCTTCAA	66	3155
1055209	N/A	N/A	226997	227016	TTGGTTATTTACTCATTCTA	20	3156
1055215	N/A	N/A	227006	227025	TCCATAAACTTGGTTATTTA	25	3157
1055221	N/A	N/A	251494	251513	TTAGCTTTTCAAATACTAAA	91	3158
1055227	N/A	N/A	251503	251522	TCAGCATACTTAGCTTTTCA	11	3159
1055232	N/A	N/A	251510	251529	GACAGTGTCAGCATACTTAG	12	3160
1055238	N/A	N/A	273793	273812	TACCCAGGTTATTACACTGT	116	3161
1055244	N/A	N/A	284229	284248	TTGGGTTTTTCTGTACAAAG	1	3162
1055249	N/A	N/A	284235	284254	TTTTGTTTGGGTTTTTCTGT	1	3163
1055255	N/A	N/A	284335	284354	CTAGTTCTTATCACTATTCA	7	3164
1055260	N/A	N/A	284342	284361	ATGTCAACTAGTTCTTATCA	5	3165
1055266	N/A	N/A	284351	284370	GACTAAACAATGTCAACTAG	12	3166
1055272	N/A	N/A	291011	291030	TGGGTTTTTAGTTTTCCTTC	4	3167
1055277	N/A	N/A	291017	291036	AGGTCCTGGGTTTTTAGTTT	3	3168
1055283	N/A	N/A	296997	297016	TAAATGACTGTGGTGCAGCC	9	3169
1055294	N/A	N/A	297013	297032	AAGCCAGTGTTTGCATTAAA	1	3170
1055300	N/A	N/A	306737	306756	AAGGGCCACTAAATCTGACC	22	3171
1055306	N/A	N/A	318477	318496	ATTTCTTTTTTTTTAAGTT	103	3172
1055311	N/A	N/A	318486	318505	GTGTTTGATATTTCTTTTTT	1	3173
1055317	N/A	N/A	318495	318514	CTTTCAAATGTGTTTGATAT	3	3174
1055323	N/A	N/A	332356	332375	TTATAACAATTTGCATAGTC	4	3175
1055328	N/A	N/A	332363	332382	GGGAGTATTATAACAATTTG	1	3176
1055334	N/A	N/A	332372	332391	TATTTTCCAGGGAGTATTAT	36	3177
1055340	N/A	N/A	347819	347838	CATTATCTAGTTTCTGGAAA	28	3178
1055345	N/A	N/A	347825	347844	AATGGTCATTATCTAGTTTC	7	3179
1055351	N/A	N/A	353593	353612	CTAAATCTGACTTACAAAGG	121	3180
1055357	N/A	N/A	377459	377478	TAAAACCAATACATTAACAT	117	3181
1055363	N/A	N/A	410197	410216	CATTATGCTTTAAGATCACA	5	3182

Table 43

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994311	103	122	2613	2632	TGCTGTTGCTCTGGCTGCTG	33	257
994313	111	130	2621	2640	CTTGCGGCTGCTGTTGCTCT	14	413
994328	562	581	178172	178191	ACCATAAGCTATCAGTTCCT	2	337
994599	204	223	9920	9939	GTGCTTGTAGTAGTTTTTGT	23	293
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	1	138
994701	N/A	N/A	203893	203912	GTTTGTTTAGATTTATCCTC	2	150
994717	N/A	N/A	251504	251523	GTCAGCATACTTAGCTTTTC	8	152
1040945	N/A	N/A	179793	179812	CATAGTTATATTTAATCATG	52	828
1054956	119	138	2629	2648	AACAATGTCTTGCGGCTGCT	24	3183
1054962	243	262	10654	10673	TGACTTGATGCACGATGCTC	10	3184
1054967	249	268	10660	10679	CCCTGGTGACTTGATGCACG	23	3185
1054973	554	573	178164	178183	CTATCAGTTCCTTGCAGCAG	3	3186
1054984	570	589	178180	178199	AATGGAGAACCATAAGCTAT	26	3187
1054990	587	606	178197	178216	CCATGTGCTTTCATCACAAT	20	3188
1054995	593	612	N/A	N/A	ACTGTACCATGTGCTTTCAT	1	3189
1055001	5489	5508	459742	459761	TTCAGTTTAGTTGCAGCCAT	7	3190
1055005	5498	5517	459751	459770	AGGTATTTGTTCAGTTTAGT	7	3191
1055009	5505	5524	459758	459777	AAAAGTCAGGTATTTGTTCA	15	3192
1055015	6030	6049	460283	460302	TGGTTTAGTGGATCCAGTCA	18	3193
1055019	6036	6055	460289	460308	TAGTGTTGGTTTAGTGGATC	23	3194
1055024	9476	9495	463729	463748	TGTTGTTATTGTATAGATAC	9	3195
1055030	9485	9504	463738	463757	CTTAGAGATTGTTGTTATTG	15	3196
1055035	9492	9511	463745	463764	GGAAATTCTTAGAGATTGTT	12	3197
1055040	10092	10111	464345	464364	AATGATCTGATATTAAAACA	43	3198
1055045	10098	10117	464351	464370	GTGGGTAATGATCTGATATT	13	3199
1055051	188	207	N/A	N/A	TTGTGAGGTAAAACTGTAAA	137	3200
1055057	197	216	9913	9932	TAGTAGTTTTTGTGAGGTAA	12	3201
1055065	N/A	N/A	17722	17741	CCTTTTCTATTTGCACTAGC	28	3202
1055071	N/A	N/A	17729	17748	AATGTCACCTTTTCTATTTG	16	3203
1055077	N/A	N/A	36482	36501	AACTCTCTTAAGTACTTATA	16	3204
1055083	N/A	N/A	85510	85529	TATGCTATGCTCACAGAGAA	55	3205
1055088	N/A	N/A	85517	85536	AGTTTGATATGCTATGCTCA	8	3206
1055094	N/A	N/A	85526	85545	CTTACAGTTAGTTTGATATG	26	3207
1055099	N/A	N/A	125427	125446	AGCTTCCAGATAAAACCTCC	61	3208
1055105	N/A	N/A	179272	179291	TTCAAAATTCTCAGCATTGG	5	3209
1055111	N/A	N/A	179787	179806	TATATTTAATCATGTTCCCG	13	3210
1055121	N/A	N/A	184178	184197	TTATATGTATACAATTCTGA	67	3211
1055126	N/A	N/A	184185	184204	CTCAGGTTTATATGTATACA	1	3212

1055132	N/A	N/A	184194	184213	GGCAATGTTCTCAGGTTTAT	1	3213
1055138	N/A	N/A	203034	203053	TCCTTTCTTCTTTGTTCATA	9	3214
1055143	N/A	N/A	203040	203059	TCTTGTTCCTTTCTTCTTTG	20	3215
1055149	N/A	N/A	203885	203904	AGATTTATCCTCAGGATGCA	26	3216
1055160	N/A	N/A	210726	210745	TAATACTCCATTTTTCCTTC	25	3217
1055165	N/A	N/A	210732	210751	AATGTGTAATACTCCATTTT	51	3218
1055171	N/A	N/A	212021	212040	TCATTTCTCTCTGGCTGTGC	27	3219
1055177	N/A	N/A	212030	212049	CTATGTTAGTCATTTCTCTC	15	3220
1055182	N/A	N/A	212037	212056	ATCAAGTCTATGTTAGTCAT	11	3221
1055188	N/A	N/A	217278	217297	TTTAAGGTATTTTCATGGAG	7	3222
1055193	N/A	N/A	217285	217304	AGTTATGTTTAAGGTATTTT	53	3223
1055199	N/A	N/A	217294	217313	ACTTGTAACAGTTATGTTTA	44	3224
1055205	N/A	N/A	226992	227011	TATTTACTCATTCTACCTTC	63	3225
1055210	N/A	N/A	226998	227017	CTTGGTTATTTACTCATTCT	21	3226
1055216	N/A	N/A	228677	228696	GGCTGATTCTAGTACTGTGA	51	3227
1055222	N/A	N/A	251496	251515	ACTTAGCTTTTCAAATACTA	30	3228
1055233	N/A	N/A	251512	251531	AGGACAGTGTCAGCATACTT	14	3229
1055239	N/A	N/A	284221	284240	TTCTGTACAAAGTTCAGTTG	54	3230
1055245	N/A	N/A	284230	284249	TTTGGGTTTTTCTGTACAAA	<1	3231
1055250	N/A	N/A	284237	284256	AGTTTTGTTTGGGTTTTTCT	<1	3232
1055256	N/A	N/A	284337	284356	AACTAGTTCTTATCACTATT	37	3233
1055261	N/A	N/A	284343	284362	AATGTCAACTAGTTCTTATC	2	3234
1055267	N/A	N/A	288842	288861	TATAAAATTCACCTAAAATT	110	3235
1055273	N/A	N/A	291012	291031	CTGGGTTTTTAGTTTTCCTT	1	3236
1055278	N/A	N/A	291018	291037	TAGGTCCTGGGTTTTTAGTT	3	3237
1055284	N/A	N/A	296999	297018	ATTAAATGACTGTGGTGCAG	3	3238
1055289	N/A	N/A	297006	297025	TGTTTGCATTAAATGACTGT	27	3239
1055295	N/A	N/A	297015	297034	AAAAGCCAGTGTTTGCATTA	2	3240
1055301	N/A	N/A	306738	306757	TAAGGGCCACTAAATCTGAC	12	3241
			306824	306843			
1055307	N/A	N/A	318479	318498	ATATTTCTTTTTTTTTTAAG	134	3242
1055312	N/A	N/A	318487	318506	TGTGTTTGATATTTCTTTTT	<1	3243
1055318	N/A	N/A	318632	318651	ATGCAAGGTCCAGGGAATAC	1	3244
1055324	N/A	N/A	332358	332377	TATTATAACAATTTGCATAG	46	3245
1055329	N/A	N/A	332364	332383	AGGGAGTATTATAACAATTT	1	3246
1055335	N/A	N/A	333552	333571	TATGAGTAATTAGCACAAAG	11	3247
1055341	N/A	N/A	347820	347839	TCATTATCTAGTTTCTGGAA	6	3248
1055346	N/A	N/A	347826	347845	AAATGGTCATTATCTAGTTT	5	3249
1055352	N/A	N/A	353767	353786	ACTTCCAATTTTGAAATACT	10	3250
1055358	N/A	N/A	389235	389254	GAAAGCCCCAGCACATAAAT	114	3251
1055364	N/A	N/A	420350	420369	TGAAAGCTGGCCGATATCCC	65	3252

Table 44

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994312	105	124	2615	2634	GCTGCTGTTGCTCTGGCTGC	48	335
994447	5491	5510	459744	459763	TGTTCAGTTTAGTTGCAGCC	12	274
994449	5499	5518	459752	459771	CAGGTATTTGTTCAGTTTAG	8	430
994561	9486	9505	463739	463758	TCTTAGAGATTGTTGTTATT	13	444
994597	198	217	9914	9933	GTAGTAGTTTTTGTGAGGTA	10	137
994601	206	225	9922	9941	TGGTGCTTGTAGTAGTTTTT	31	449
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
994703	N/A	N/A	212031	212050	TCTATGTTAGTCATTTCTCT	21	306
994731	N/A	N/A	284231	284250	GTTTGGGTTTTTCTGTACAA	2	621
1040848	N/A	N/A	96129	96148	CACTTTCTAGATTATTCTTA	102	748
1054951	112	131	2622	2641	TCTTGCGGCTGCTGTTGCTC	14	3253
1054957	121	140	2631	2650	GAAACAATGTCTTGCGGCTG	15	3254
1054963	244	263	10655	10674	GTGACTTGATGCACGATGCT	8	3255
1054968	250	269	10661	10680	ACCCTGGTGACTTGATGCAC	20	3256
1054974	556	575	178166	178185	AGCTATCAGTTCCTTGCAGC	11	3257
1054979	563	582	178173	178192	AACCATAAGCTATCAGTTCC	7	3258
1054985	572	591	178182	178201	ACAATGGAGAACCATAAGCT	101	3259
1054991	588	607	178198	178217	ACCATGTGCTTTCATCACAA	3	3260
1054996	594	613	N/A	N/A	AACTGTACCATGTGCTTTCA	3	3261
1055010	5507	5526	459760	459779	AGAAAAGTCAGGTATTTGTT	14	3262
1055016	6031	6050	460284	460303	TTGGTTTAGTGGATCCAGTC	31	3263
1055020	6037	6056	460290	460309	TTAGTGTTGGTTTAGTGGAT	20	3264
1055025	9478	9497	463731	463750	ATTGTTGTTATTGTATAGAT	18	3265
1055036	9494	9513	463747	463766	ATGGAAATTCTTAGAGATTG	16	3266
1055041	10093	10112	464346	464365	TAATGATCTGATATTAAAAC	111	3267
1055046	10099	10118	464352	464371	GGTGGGTAATGATCTGATAT	34	3268
1055052	190	209	N/A	N/A	TTTTGTGAGGTAAAACTGTA	136	3269
1055066	N/A	N/A	17723	17742	ACCTTTTCTATTTGCACTAG	19	3270
1055072	N/A	N/A	17730	17749	AAATGTCACCTTTTCTATTT	56	3271
1055078	N/A	N/A	36986	37005	GCTATTTTTTCCAGAAAGTC	6	3272
1055084	N/A	N/A	85512	85531	GATATGCTATGCTCACAGAG	23	3273
1055089	N/A	N/A	85518	85537	TAGTTTGATATGCTATGCTC	33	3274
1055100	N/A	N/A	133992	134011	AATTTTTTTTAACATCTTGC	88	3275
1055106	N/A	N/A	179779	179798	ATCATGTTCCCGATATTGGA	15	3276
1055112	N/A	N/A	179788	179807	TTATATTTAATCATGTTCCC	11	3277
1055116	N/A	N/A	179795	179814	AACATAGTTATATTTAATCA	132	3278
1055122	N/A	N/A	184180	184199	GTTTATATGTATACAATTCT	26	3279
1055127	N/A	N/A	184186	184205	TCTCAGGTTTATATGTATAC	4	3280
1055133	N/A	N/A	187811	187830	TCACAGGGAATAATGAAGAG	73	3281

1055139	N/A	N/A	203035	203054	TTCCTTTCTTCTTTGTTCAT	45	3282
1055144	N/A	N/A	203041	203060	CTCTTGTTCCTTTCTTCTTT	20	3283
1055150	N/A	N/A	203887	203906	TTAGATTTATCCTCAGGATG	51	3284
1055155	N/A	N/A	203894	203913	GGTTTGTTTAGATTTATCCT	11	3285
1055161	N/A	N/A	210727	210746	GTAATACTCCATTTTTCCTT	4	3286
1055166	N/A	N/A	210733	210752	AAATGTGTAATACTCCATTT	53	3287
1055172	N/A	N/A	212023	212042	AGTCATTTCTCTCTGGCTGT	53	3288
1055183	N/A	N/A	212039	212058	AAATCAAGTCTATGTTAGTC	63	3289
1055189	N/A	N/A	217280	217299	TGTTTAAGGTATTTTCATGG	8	3290
1055194	N/A	N/A	217286	217305	CAGTTATGTTTAAGGTATTT	19	3291
1055200	N/A	N/A	222603	222622	CTGTTCTTAGCTTCCCAGCT	39	3292
1055206	N/A	N/A	226993	227012	TTATTTACTCATTCTACCTT	82	3293
1055211	N/A	N/A	226999	227018	ACTTGGTTATTTACTCATTC	17	3294
1055217	N/A	N/A	230285	230304	AATCTCCAGTTATGAGTAAG	82	3295
1055223	N/A	N/A	251498	251517	ATACTTAGCTTTTCAAATAC	83	3296
1055228	N/A	N/A	251505	251524	TGTCAGCATACTTAGCTTTT	32	3297
1055234	N/A	N/A	251514	251533	CCAGGACAGTGTCAGCATAC	29	3298
1055240	N/A	N/A	284223	284242	TTTTCTGTACAAAGTTCAGT	4	3299
1055251	N/A	N/A	284239	284258	TTAGTTTTGTTTGGGTTTTT	2	3300
1055257	N/A	N/A	284338	284357	CAACTAGTTCTTATCACTAT	15	3301
1055262	N/A	N/A	284344	284363	CAATGTCAACTAGTTCTTAT	4	3302
1055268	N/A	N/A	291004	291023	TTAGTTTTCCTTCTTGTCTT	7	3303
1055274	N/A	N/A	291013	291032	CCTGGGTTTTTAGTTTTCCT	3	3304
1055279	N/A	N/A	291020	291039	ATTAGGTCCTGGGTTTTTAG	3	3305
1055285	N/A	N/A	297001	297020	GCATTAAATGACTGTGGTGC	5	3306
1055290	N/A	N/A	297007	297026	GTGTTTGCATTAAATGACTG	4	3307
1055296	N/A	N/A	306730	306749	ACTAAATCTGACCTTCCTCA	35	3308
1055302	N/A	N/A	306741	306760	TGGTAAGGGCCACTAAATCT	4	3309
			306827	306846			
1055308	N/A	N/A	318481	318500	TGATATTTCTTTTTTTTTTA	104	3310
1055313	N/A	N/A	318488	318507	ATGTGTTTGATATTTCTTTT	1	3311
1055319	N/A	N/A	324476	324495	TGATCTAAATTGTGTCTTTT	17	3312
1055325	N/A	N/A	332359	332378	GTATTATAACAATTTGCATA	6	3313
1055330	N/A	N/A	332365	332384	CAGGGAGTATTATAACAATT	2	3314
1055336	N/A	N/A	334250	334269	TCATAGAAGCATTCTGTGTT	90	3315
1055342	N/A	N/A	347821	347840	GTCATTATCTAGTTTCTGGA	2	3316
1055347	N/A	N/A	347827	347846	CAAATGGTCATTATCTAGTT	10	3317
1055353	N/A	N/A	355980	355999	ATCTGCTAGGCATGCGGGAT	27	3318
1055359	N/A	N/A	396488	396507	TGATTTGTACACACCCAGCA	62	3319
1055365	N/A	N/A	432459	432478	GCACTGATCCAATAAAACCC	93	3320

Table 45

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	2	138
994690	N/A	N/A	179789	179808	GTTATATTTAATCATGTTCC	4	538
994734	N/A	N/A	291014	291033	TCCTGGGTTTTTAGTTTTCC	2	232
1041358	N/A	N/A	438300	438319	GAGAGTATAAAAATTATCTC	93	3073
1054947	107	126	2617	2636	CGGCTGCTGTTGCTCTGGCT	25	3321
1054952	113	132	2623	2642	GTCTTGCGGCTGCTGTTGCT	16	3322
1054964	245	264	10656	10675	GGTGACTTGATGCACGATGC	7	3323
1054969	252	271	10663	10682	CCACCCTGGTGACTTGATGC	13	3324
1054975	558	577	178168	178187	TAAGCTATCAGTTCCTTGCA	5	3325
1054980	564	583	178174	178193	GAACCATAAGCTATCAGTTC	24	3326
1054986	580	599	178190	178209	CTTTCATCACAATGGAGAAC	101	3327
1054992	589	608	178199	178218	TACCATGTGCTTTCATCACA	6	3328
1054997	596	615	N/A	N/A	AAAACTGTACCATGTGCTTT	4	3329
1055002	5493	5512	459746	459765	TTTGTTCAGTTTAGTTGCAG	17	3330
1055006	5500	5519	459753	459772	TCAGGTATTTGTTCAGTTTA	6	3331
1055011	5509	5528	459762	459781	AAAGAAAAGTCAGGTATTTG	42	3332
1055017	6032	6051	460285	460304	GTTGGTTTAGTGGATCCAGT	42	3333
1055021	6038	6057	460291	460310	CTTAGTGTTGGTTTAGTGGA	28	3334
1055026	9480	9499	463733	463752	AGATTGTTGTTATTGTATAG	20	3335
1055031	9487	9506	463740	463759	TTCTTAGAGATTGTTGTTAT	20	3336
1055037	9496	9515	463749	463768	TTATGGAAATTCTTAGAGAT	67	3337
1055042	10094	10113	464347	464366	GTAATGATCTGATATTAAAA	54	3338
1055047	10100	10119	464353	464372	TGGTGGGTAATGATCTGATA	14	3339
1055053	192	211	N/A	N/A	GTTTTTGTGAGGTAAAACTG	111	3340
1055058	199	218	9915	9934	TGTAGTAGTTTTTGTGAGGT	19	3341
1055061	208	227	9924	9943	CTTGGTGCTTGTAGTAGTTT	25	3342
1055067	N/A	N/A	17724	17743	CACCTTTTCTATTTGCACTA	23	3343
1055073	N/A	N/A	17732	17751	TCAAATGTCACCTTTTCTAT	52	3344
1055079	N/A	N/A	49576	49595	ATAGCAAGTCCCCTGAAGCT	83	3345
1055085	N/A	N/A	85513	85532	TGATATGCTATGCTCACAGA	25	3346
1055090	N/A	N/A	85519	85538	TTAGTTTGATATGCTATGCT	36	3347
1055095	N/A	N/A	99353	99372	CACAGAACACTTTTTCCAGA	41	3348
1055101	N/A	N/A	144499	144518	ATCACACAGCAGCATGTTTA	72	3349
1055107	N/A	N/A	179781	179800	TAATCATGTTCCCGATATTG	21	3350
1055117	N/A	N/A	179797	179816	CTAACATAGTTATATTTAAT	121	3351
1055123	N/A	N/A	184181	184200	GGTTTATATGTATACAATTC	3	3352
1055128	N/A	N/A	184187	184206	TTCTCAGGTTTATATGTATA	5	3353
1055134	N/A	N/A	203027	203046	TTCTTTGTTCATAGGAGAAC	91	3354
1055140	N/A	N/A	203036	203055	GTTCCTTTCTTCTTTGTTCA	17	3355

1055145	N/A	N/A	203043	203062	ACCTCTTGTTCCTTTCTTCT	10	3356
1055151	N/A	N/A	203889	203908	GTTTAGATTTATCCTCAGGA	3	3357
1055156	N/A	N/A	203895	203914	GGGTTTGTTTAGATTTATCC	19	3358
1055162	N/A	N/A	210728	210747	TGTAATACTCCATTTTTCCT	15	3359
1055167	N/A	N/A	210734	210753	CAAATGTGTAATACTCCATT	16	3360
1055173	N/A	N/A	212025	212044	TTAGTCATTTCTCTCTGGCT	50	3361
1055178	N/A	N/A	212032	212051	GTCTATGTTAGTCATTTCTC	13	3362
1055184	N/A	N/A	212041	212060	AAAAATCAAGTCTATGTTAG	118	3363
1055190	N/A	N/A	217281	217300	ATGTTTAAGGTATTTTCATG	41	3364
1055195	N/A	N/A	217287	217306	ACAGTTATGTTTAAGGTATT	39	3365
1055201	N/A	N/A	226199	226218	AAAACAGACTTCGATTTGGA	70	3366
1055207	N/A	N/A	226994	227013	GTTATTTACTCATTCTACCT	42	3367
1055212	N/A	N/A	227000	227019	AACTTGGTTATTTACTCATT	25	3368
1055218	N/A	N/A	233991	234010	AAGTTGGAGAAGTCACCAGC	103	3369
1055224	N/A	N/A	251500	251519	GCATACTTAGCTTTTCAAAT	6	3370
1055229	N/A	N/A	251506	251525	GTGTCAGCATACTTAGCTTT	27	3371
1055235	N/A	N/A	254560	254579	TCTTGGAGGTGACATTTGTG	55	3372
1055241	N/A	N/A	284225	284244	GTTTTTCTGTACAAAGTTCA	2	3373
1055246	N/A	N/A	284232	284251	TGTTTGGGTTTTTCTGTACA	1	3374
1055252	N/A	N/A	284241	284260	CTTTAGTTTTGTTTGGGTTT	2	3375
1055258	N/A	N/A	284339	284358	TCAACTAGTTCTTATCACTA	4	3376
1055263	N/A	N/A	284345	284364	ACAATGTCAACTAGTTCTTA	2	3377
1055269	N/A	N/A	291006	291025	TTTTAGTTTTCCTTCTTGTC	5	3378
1055280	N/A	N/A	291022	291041	AGATTAGGTCCTGGGTTTTT	2	3379
1055286	N/A	N/A	297002	297021	TGCATTAAATGACTGTGGTG	4	3380
1055291	N/A	N/A	297008	297027	AGTGTTTGCATTAAATGACT	5	3381
1055297	N/A	N/A	306732	306751	CCACTAAATCTGACCTTCCT	37	3382
1055303	N/A	N/A	306746	306765	TCCATTGGTAAGGGCCACTA	2	3383
1055309	N/A	N/A	318483	318502	TTTGATATTTCTTTTTTTTT	96	3384
1055314	N/A	N/A	318489	318508	AATGTGTTTGATATTTCTTT	1	3385
1055320	N/A	N/A	326832	326851	CAGTTTTGAGATGGTTTGAA	3	3386
1055326	N/A	N/A	332360	332379	AGTATTATAACAATTTGCAT	22	3387
1055331	N/A	N/A	332366	332385	CCAGGGAGTATTATAACAAT	2	3388
1055337	N/A	N/A	347813	347832	CTAGTTTCTGGAAAGTAATG	36	3389
1055343	N/A	N/A	347822	347841	GGTCATTATCTAGTTTCTGG	1	3390
1055348	N/A	N/A	347829	347848	AACAAATGGTCATTATCTAG	9	3391
1055354	N/A	N/A	358326	358345	CCAAATTCCTGGTTGCTGTG	4	3392
1055360	N/A	N/A	397561	397580	AGGGCCTCTTGGATTTTGTT	130	3393

Table 46

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994314	246	265	10657	10676	TGGTGACTTGATGCACGATG	12	491
994329	590	609	178200	178219	GTACCATGTGCTTTCATCAC	5	415
994465	6033	6052	460286	460305	TGTTGGTTTAGTGGATCCAG	21	432
994467	6040	6059	460293	460312	ATCTTAGTGTTGGTTTAGTG	20	588
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	4	138
994700	N/A	N/A	203037	203056	TGTTCCTTTCTTCTTTGTTC	10	72
994761	N/A	N/A	347823	347842	TGGTCATTATCTAGTTTCTG	2	469
1054948	108	127	2618	2637	GCGGCTGCTGTTGCTCTGGC	57	3394
1054953	114	133	2624	2643	TGTCTTGCGGCTGCTGTTGC	16	3395
1054970	254	273	10665	10684	GACCACCCTGGTGACTTGAT	9	3396
1054976	559	578	178169	178188	ATAAGCTATCAGTTCCTTGC	11	3397
1054981	565	584	178175	178194	AGAACCATAAGCTATCAGTT	7	3398
1054987	582	601	178192	178211	TGCTTTCATCACAATGGAGA	62	3399
1054998	598	617	N/A	N/A	GGAAAACTGTACCATGTGCT	4	3400
1055003	5495	5514	459748	459767	TATTTGTTCAGTTTAGTTGC	9	3401
1055007	5501	5520	459754	459773	GTCAGGTATTTGTTCAGTTT	9	3402
1055012	6024	6043	460277	460296	AGTGGATCCAGTCAATTCAA	34	3403
1055027	9482	9501	463735	463754	AGAGATTGTTGTTATTGTAT	16	3404
1055032	9488	9507	463741	463760	ATTCTTAGAGATTGTTGTTA	21	3405
1055038	10086	10105	464339	464358	CTGATATTAAAACATCCAGT	21	3406
1055043	10095	10114	464348	464367	GGTAATGATCTGATATTAAA	15	3407
1055048	10102	10121	464355	464374	TATGGTGGGTAATGATCTGA	16	3408
1055054	194	213	9910	9929	TAGTTTTTGTGAGGTAAAAC	83	3409
1055059	200	219	9916	9935	TTGTAGTAGTTTTTGTGAGG	28	3410
1055062	N/A	N/A	17716	17735	CTATTTGCACTAGCTGCCTA	75	3411
1055068	N/A	N/A	17725	17744	TCACCTTTTCTATTTGCACT	10	3412
1055074	N/A	N/A	17734	17753	TCTCAAATGTCACCTTTTCT	44	3413
1055080	N/A	N/A	54036	54055	AACCATATGACATCTCAACA	33	3414
1055086	N/A	N/A	85514	85533	TTGATATGCTATGCTCACAG	18	3415
1055091	N/A	N/A	85520	85539	GTTAGTTTGATATGCTATGC	36	3416
1055096	N/A	N/A	103883	103902	CAACTGAAAATTCTACACAC	110	3417
1055102	N/A	N/A	147181	147200	CAGTAGTCTCCCCATAGCCA	76	3418
1055108	N/A	N/A	179783	179802	TTTAATCATGTTCCCGATAT	57	3419
1055113	N/A	N/A	179790	179809	AGTTATATTTAATCATGTTC	17	3420
1055118	N/A	N/A	179799	179818	CACTAACATAGTTATATTTA	72	3421
1055124	N/A	N/A	184182	184201	AGGTTTATATGTATACAATT	13	3422
1055129	N/A	N/A	184188	184207	GTTCTCAGGTTTATATGTAT	5	3423
1055135	N/A	N/A	203029	203048	TCTTCTTTGTTCATAGGAGA	147	3424
1055146	N/A	N/A	203045	203064	CAACCTCTTGTTCCTTTCTT	52	3425

1055152	N/A	N/A	203890	203909	TGTTTAGATTTATCCTCAGG	5	3426
1055157	N/A	N/A	210720	210739	TCCATTTTTCCTTCTAGATT	19	3427
1055163	N/A	N/A	210729	210748	GTGTAATACTCCATTTTTCC	5	3428
1055168	N/A	N/A	210736	210755	TACAAATGTGTAATACTCCA	6	3429
1055174	N/A	N/A	212027	212046	TGTTAGTCATTTCTCTCTGG	23	3430
1055179	N/A	N/A	212033	212052	AGTCTATGTTAGTCATTTCT	24	3431
1055185	N/A	N/A	213048	213067	GATGATAAATTAAGGCAGAG	22	3432
1055191	N/A	N/A	217282	217301	TATGTTTAAGGTATTTTCAT	47	3433
1055196	N/A	N/A	217288	217307	AACAGTTATGTTTAAGGTAT	43	3434
1055202	N/A	N/A	226986	227005	CTCATTCTACCTTCAACTCT	94	3435
1055208	N/A	N/A	226995	227014	GGTTATTTACTCATTCTACC	14	3436
1055213	N/A	N/A	227002	227021	TAAACTTGGTTATTTACTCA	79	3437
1055219	N/A	N/A	236034	236053	GAGTGAGCATTAGATGGTCA	56	3438
1055225	N/A	N/A	251501	251520	AGCATACTTAGCTTTTCAAA	10	3439
1055230	N/A	N/A	251507	251526	AGTGTCAGCATACTTAGCTT	16	3440
1055236	N/A	N/A	257663	257682	AGGGAAATGGTCATTTTCTA	87	3441
1055242	N/A	N/A	284227	284246	GGGTTTTTCTGTACAAAGTT	4	3442
1055247	N/A	N/A	284233	284252	TTGTTTGGGTTTTTCTGTAC	3	3443
1055253	N/A	N/A	284331	284350	TTCTTATCACTATTCAGTCA	3	3444
1055259	N/A	N/A	284340	284359	GTCAACTAGTTCTTATCACT	2	3445
1055264	N/A	N/A	284347	284366	AAACAATGTCAACTAGTTCT	12	3446
1055270	N/A	N/A	291008	291027	GTTTTTAGTTTTCCTTCTTG	3	3447
1055275	N/A	N/A	291015	291034	GTCCTGGGTTTTTAGTTTTC	2	3448
1055281	N/A	N/A	291024	291043	GAAGATTAGGTCCTGGGTTT	5	3449
1055287	N/A	N/A	297003	297022	TTGCATTAAATGACTGTGGT	2	3450
1055292	N/A	N/A	297009	297028	CAGTGTTTGCATTAAATGAC	3	3451
1055298	N/A	N/A	306734	306753	GGCCACTAAATCTGACCTTC	54	3452
1055304	N/A	N/A	306748	306767	AATCCATTGGTAAGGGCCAC	4	3453
1055310	N/A	N/A	318484	318503	GTTTGATATTTCTTTTTTTT	2	3454
1055315	N/A	N/A	318491	318510	CAAATGTGTTTGATATTTCT	3	3455
1055321	N/A	N/A	332352	332371	AACAATTTGCATAGTCTCTC	3	3456
1055327	N/A	N/A	332361	332380	GAGTATTATAACAATTTGCA	3	3457
1055332	N/A	N/A	332368	332387	TTCCAGGGAGTATTATAACA	2	3458
1055338	N/A	N/A	347815	347834	ATCTAGTTTCTGGAAAGTAA	22	3459
1055349	N/A	N/A	347831	347850	ATAACAAATGGTCATTATCT	43	3460
1055355	N/A	N/A	365965	365984	AATCCAAATCTTGTATTCTT	9	3461
1055361	N/A	N/A	399995	400014	TCTAGAAATGATTTTGATTA	107	3462
1055366	N/A	N/A	439847	439866	TGGGCATTTAAGAAATGCTC	140	3463

Table 47

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 1 Start Site	SEQ ID NO: 1 Stop Site	SEQ ID NO: 2 Start Site	SEQ ID NO: 2 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
994448	5496	5515	459749	459768	GTATTTGTTCAGTTTAGTTG	9	352
994466	6034	6053	460287	460306	GTGTTGGTTTAGTGGATCCA	21	510
994571	10096	10115	464349	464368	GGGTAATGATCTGATATTAA	10	601
994598	201	220	9917	9936	CTTGTAGTAGTTTTTGTGAG	42	215
994605	N/A	N/A	17726	17745	GTCACCTTTTCTATTTGCAC	3	138
994702	N/A	N/A	210730	210749	TGTGTAATACTCCATTTTTC	8	228
994713	N/A	N/A	226996	227015	TGGTTATTTACTCATTCTAC	10	463
994732	N/A	N/A	284341	284360	TGTCAACTAGTTCTTATCAC	3	76
994743	N/A	N/A	318485	318504	TGTTTGATATTTCTTTTTTT	3	311
994756	N/A	N/A	332362	332381	GGAGTATTATAACAATTTGC	1	79
1040299	5502	5521	459755	459774	AGTCAGGTATTTGTTCAGTT	6	2809
1040631	10088	10107	464341	464360	ATCTGATATTAAAACATCCA	18	1280
1054949	109	128	2619	2638	TGCGGCTGCTGTTGCTCTGG	22	3464
1054954	115	134	2625	2644	ATGTCTTGCGGCTGCTGTTG	10	3465
1054965	247	266	10658	10677	CTGGTGACTTGATGCACGAT	21	3466
1054971	256	275	10667	10686	TGGACCACCCTGGTGACTTG	17	3467
1054977	560	579	178170	178189	CATAAGCTATCAGTTCCTTG	5	3468
1054982	566	585	178176	178195	GAGAACCATAAGCTATCAGT	11	3469
1054988	584	603	178194	178213	TGTGCTTTCATCACAATGGA	56	3470
1054993	591	610	178201	178220	TGTACCATGTGCTTTCATCA	3	3471
1054999	600	619	N/A	N/A	TTGGAAAACTGTACCATGTG	8	3472
1055013	6026	6045	460279	460298	TTAGTGGATCCAGTCAATTC	31	3473
1055022	6042	6061	460295	460314	CCATCTTAGTGTTGGTTTAG	23	3474
1055028	9483	9502	463736	463755	TAGAGATTGTTGTTATTGTA	14	3475
1055033	9489	9508	463742	463761	AATTCTTAGAGATTGTTGTT	19	3476
1055049	10104	10123	464357	464376	CATATGGTGGGTAATGATCT	62	3477
1055055	195	214	9911	9930	GTAGTTTTTGTGAGGTAAAA	8	3478
1055063	N/A	N/A	17718	17737	TTCTATTTGCACTAGCTGCC	78	3479
1055069	N/A	N/A	17727	17746	TGTCACCTTTTCTATTTGCA	2	3480
1055075	N/A	N/A	17736	17755	CCTCTCAAATGTCACCTTTT	85	3481
1055081	N/A	N/A	85506	85525	CTATGCTCACAGAGAACCTG	98	3482
1055087	N/A	N/A	85515	85534	TTTGATATGCTATGCTCACA	13	3483
1055092	N/A	N/A	85522	85541	CAGTTAGTTTGATATGCTAT	25	3484
1055097	N/A	N/A	103952	103971	TGTGATTTATCGCTGACCTT	53	3485
1055103	N/A	N/A	148568	148587	GAATGGTTCTCTTTTACGGG	8	3486
1055109	N/A	N/A	179785	179804	TATTTAATCATGTTCCCGAT	19	3487
1055114	N/A	N/A	179791	179810	TAGTTATATTTAATCATGTT	63	3488
1055119	N/A	N/A	184174	184193	ATGTATACAATTCTGACAGT	49	3489
1055125	N/A	N/A	184183	184202	CAGGTTTATATGTATACAAT	5	3490

1055130	N/A	N/A	184190	184209	ATGTTCTCAGGTTTATATGT	5	3491
1055136	N/A	N/A	203031	203050	TTTCTTCTTTGTTCATAGGA	71	3492
1055141	N/A	N/A	203038	203057	TTGTTCCTTTCTTCTTTGTT	46	3493
1055147	N/A	N/A	203047	203066	AACAACCTCTTGTTCCTTTC	13	3494
1055153	N/A	N/A	203891	203910	TTGTTTAGATTTATCCTCAG	6	3495
1055158	N/A	N/A	210722	210741	ACTCCATTTTTCCTTCTAGA	6	3496
1055169	N/A	N/A	210738	210757	ATTACAAATGTGTAATACTC	62	3497
1055175	N/A	N/A	212028	212047	ATGTTAGTCATTTCTCTCTG	20	3498
1055180	N/A	N/A	212034	212053	AAGTCTATGTTAGTCATTTC	31	3499
1055186	N/A	N/A	217274	217293	AGGTATTTTCATGGAGTTTC	3	3500
1055192	N/A	N/A	217283	217302	TTATGTTTAAGGTATTTTCA	60	3501
1055197	N/A	N/A	217290	217309	GTAACAGTTATGTTTAAGGT	8	3502
1055203	N/A	N/A	226988	227007	TACTCATTCTACCTTCAACT	72	3503
1055214	N/A	N/A	227004	227023	CATAAACTTGGTTATTTACT	65	3504
1055220	N/A	N/A	248565	248584	CCACTACCACCCCCAAACCA	53	3505
1055226	N/A	N/A	251502	251521	CAGCATACTTAGCTTTTCAA	16	3506
1055231	N/A	N/A	251508	251527	CAGTGTCAGCATACTTAGCT	20	3507
1055237	N/A	N/A	259737	259756	CATGTATTGCTAGGAGCCAG	46	3508
1055243	N/A	N/A	284228	284247	TGGGTTTTTCTGTACAAAGT	2	3509
1055248	N/A	N/A	284234	284253	TTTGTTTGGGTTTTTCTGTA	2	3510
1055254	N/A	N/A	284333	284352	AGTTCTTATCACTATTCAGT	2	3511
1055265	N/A	N/A	284349	284368	CTAAACAATGTCAACTAGTT	61	3512
1055271	N/A	N/A	291010	291029	GGGTTTTTAGTTTTCCTTCT	2	3513
1055276	N/A	N/A	291016	291035	GGTCCTGGGTTTTTAGTTTT	3	3514
1055282	N/A	N/A	296995	297014	AATGACTGTGGTGCAGCCTC	27	3515
1055288	N/A	N/A	297004	297023	TTTGCATTAAATGACTGTGG	2	3516
1055293	N/A	N/A	297011	297030	GCCAGTGTTTGCATTAAATG	2	3517
1055299	N/A	N/A	306736	306755	AGGGCCACTAAATCTGACCT	118	3518
1055305	N/A	N/A	306750	306769	AGAATCCATTGGTAAGGGCC	6	3519
1055316	N/A	N/A	318493	318512	TTCAAATGTGTTTGATATTT	12	3520
1055322	N/A	N/A	332354	332373	ATAACAATTTGCATAGTCTC	4	3521
1055333	N/A	N/A	332370	332389	TTTTCCAGGGAGTATTATAA	21	3522
1055339	N/A	N/A	347817	347836	TTATCTAGTTTCTGGAAAGT	39	3523
1055344	N/A	N/A	347824	347843	ATGGTCATTATCTAGTTTCT	2	3524
1055350	N/A	N/A	347833	347852	TGATAACAAATGGTCATTAT	32	3525
1055356	N/A	N/A	372672	372691	CATCAAAATTGTGCACAATT	81	3526
1055362	N/A	N/A	402059	402078	TGAAAACATGTTGTGTGATT	57	3527
1055367	N/A	N/A	453507	453526	TTGTTGGATTCTTTTTTTCT	27	3528

Table 48

Reduction of ATXN1 RNA by 5-10-5 MOE gapmers with mixed PO/PS linkages in A-431 Cells

Compound Number	SEQ ID NO: 3 Start Site	SEQ ID NO: 3 Stop Site	Sequence (5' to 3')	ATXN1 (% Control)	SEQ ID NO
1054961	193	212	GACTTGATGCACGATGCTCT	8	3529
1054958	187	206	ATGCACGATGCTCTGTAAAG	51	3530
1054959	189	208	TGATGCACGATGCTCTGTAA	42	3531
1054960	191	210	CTTGATGCACGATGCTCTGT	48	3532

Example 3: Effect of modified oligonucleotides on human ATXN1 RNA *in vitro,* multiple doses

Modified oligonucleotides selected from the examples above were tested at various doses in A-431 cells. Cultured A-431 cells 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 ATXN1 RNA levels were measured by quantitative real-time RTPCR. Human ATXN1 primer probe set RTS37573 was used to measure RNA levels as described above. ATXN1 levels were adjusted according to total RNA content, as measured by RIBOGREEN®. Results are presented in the tables below as percent reduction of the amount of ATXN1 RNA, relative to untreated control. Where possible, the half maximal inhibitory concentration (IC_{50}) of each modified oligonucleotide was calculated using a linear regression on a log/linear plot of the data in excel.

Table 49

Dose-dependent percent reduction of human ATXN1 RNA in A-431 cells by modified oligonucleotides

Compound No.	% Control				IC50 (μM)
	125 nM	500 nM	2000 nM	8000 nM	
994310	60	32	19	12	0.2
994316	36	15	9	9	< 0.1
994318	46	12	9	7	< 0.1
994319	31	13	8	7	< 0.1
994392	50	26	13	10	< 0.1
994421	16	8	8	10	< 0.1
994492	48	25	15	15	< 0.1
994542	55	36	25	22	0.1
994612	22	11	9	9	< 0.1
994613	30	23	15	14	< 0.1
994623	59	50	40	35	0.5
994628	21	9	7	9	< 0.1
994631	42	25	12	10	< 0.1
994645	90	78	68	56	> 8.0
994646	64	39	28	21	0.3

994652	24	11	9	9	< 0.1
994653	35	21	13	11	< 0.1
994812	31	13	9	8	< 0.1

Table 50

Dose-dependent percent reduction of human ATXN1 RNA in A-431 cells by modified oligonucleotides

Compound No.	% Control				IC50 (μM)
	125 nM	500 nM	2000 nM	8000 nM	
994315	7	6	6	7	< 0.1
994320	11	7	4	5	< 0.1
994321	42	25	13	6	< 0.1
994395	41	27	21	12	< 0.1
994609	18	9	8	7	< 0.1
994610	94	95	79	63	> 8.0
994612	23	11	9	10	< 0.1
994616	70	51	40	27	0.7
994618	60	25	16	14	0.1
994619	53	32	18	10	< 0.1
994642	52	26	16	11	< 0.1
994643	56	35	23	17	0.2
994649	39	23	19	18	< 0.1
994651	21	9	7	6	< 0.1
994656	62	35	20	14	0.2
994696	34	17	12	9	< 0.1
994698	82	58	51	36	1.9
994770	46	23	12	11	< 0.1
994913	48	30	18	12	< 0.1

Table 51

Dose-dependent percent reduction of human ATXN1 RNA by modified oligonucleotides

Compound No.	% Control				IC50 (μM)
	125 nM	500 nM	2000 nM	8000 nM	
994328	115	120	134	116	> 8.0
994597	57	24	11	10	< 0.1
994599	55	36	30	22	0.1
994612	28	12	8	12	< 0.1
994630	68	43	26	15	0.4
994638	76	40	22	15	0.4
994693	78	55	35	17	0.8
994700	12	5	4	4	< 0.1
994701	63	36	19	16	0.2
994702	50	27	16	12	< 0.1
994703	66	43	29	16	0.4

994717	11	8	9	6	< 0.1
994732	21	11	9	9	< 0.1
994734	9	4	2	2	< 0.1
994735	49	21	15	14	< 0.1
994740	67	37	20	15	0.3
994743	23	11	9	11	< 0.1
994756	39	21	13	12	< 0.1
994918	63	41	24	15	0.3

Table 52

Dose-dependent percent reduction of human ATXN1 RNA by modified oligonucleotides

Compound No.	% Control				IC50 (μM)
	125 nM	500 nM	2000 nM	8000 nM	
994313	63	31	15	9	0.2
994314	41	19	10	15	< 0.1
994329	18	7	5	5	< 0.1
994346	17	8	6	8	< 0.1
994449	28	9	8	10	< 0.1
994466	103	104	79	79	> 8.0
994474	36	14	13	11	< 0.1
994497	16	9	9	10	< 0.1
994561	34	17	12	10	< 0.1
994571	95	77	76	73	> 8.0
994612	26	12	10	9	< 0.1
994690	87	60	42	40	1.9
994697	23	10	6	5	< 0.1
994706	12	7	5	5	< 0.1
994713	79	61	24	11	0.7
994731	65	31	18	16	0.2
994761	57	25	14	14	< 0.1
994835	75	36	21	19	0.4
994848	61	33	22	16	0.2

Example 4: Design of modified oligonucleotides complementary to a human ATXN1 nucleic acid

Modified oligonucleotides were designed and synthesized as indicated in the tables below.

The compounds in table 53 are 5-10-5 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides, the 5' wing segment consists of five 2'-MOE nucleosides, and the 3' wing segment consists of five 2'-MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeddddddddddeeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'):

sooossssssssssssooss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 53

5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1342029	TGATTGTGTTCCATTGTAAA	7023	7042	461276	461295	3533
1342030	GAGTTGTCCATAGTCATGAA	4432	4451	458685	458704	3534
1342031	CGAGTTGTCCATAGTCATGA	4433	4452	458686	458705	3535
1342033	TGCACTTTTGTTTCTACAGC	N/A	N/A	441087	441106	3536
1342034	AGGCCTTGCACTTTTGTTTC	N/A	N/A	441093	441112	3537
1342035	AAGTGGCACCCGAGTTGTCC	4443	4462	458696	458715	3538
1342036	GCCTTGCACTTTTGTTTCTA	N/A	N/A	441091	441110	3539
1342037	GATTGTGTTCCATTGTAAAC	7022	7041	461275	461294	3540
1342039	GTGGATCCAGTCAATTCAAT	6023	6042	460276	460295	3541
1342040	AATAGCAGCTATTTCATGAC	N/A	N/A	439446	439465	3542
1342044	TGGATCCAGTCAATTCAATA	6022	6041	460275	460294	3543
1342045	TCAATTCAATACTCGAAGTA	6013	6032	460266	460285	3544
1342046	GGATCCAGTCAATTCAATAC	6021	6040	460274	460293	3545
1342050	CAATGACTCTTCACTCATGT	N/A	N/A	440235	440254	3546
1342051	ACTATTTTCAACTCAAGCTG	N/A	N/A	439428	439447	3547
1342052	GACTCTTCACTCATGTTTAT	N/A	N/A	440231	440250	3548
1342053	GGTACTGGCTCATCAGTTGT	N/A	N/A	444368	444387	3549
1342054	AATGACTCTTCACTCATGTT	N/A	N/A	440234	440253	3550
1342055	AGCAATGACTCTTCACTCAT	N/A	N/A	440237	440256	3551
1342057	AAGCAATGACTCTTCACTCA	N/A	N/A	440238	440257	3552
1342060	AACCAATCTATCACACCAAT	N/A	N/A	444348	444367	3553
1342063	AGCCATCCAAGTAAGAATAT	5475	5494	459728	459747	3554
1342065	ACCAATCTATCACACCAATG	N/A	N/A	444347	444366	3555
1342066	CAATCTATCACACCAATGCA	N/A	N/A	444345	444364	3556
1342068	CAGCCATCCAAGTAAGAATA	5476	5495	459729	459748	3557
1342069	TATTGTCACATACTAGTTCA	4755	4774	459008	459027	3558
1342070	CTGACTAATTTCTTGGTGAT	7039	7058	461292	461311	3559
1342074	GTGGTCATTTATTGTCACAT	4764	4783	459017	459036	3560
1342075	GTCACATACTAGTTCATAAT	4751	4770	459004	459023	3561
1342076	TTATTGTCACATACTAGTTC	4756	4775	459009	459028	3562
1342032	CCCGAGTTGTCCATAGTCAT	4435	4454	458688	458707	3563
1342038	CATTGTAAACGCAAAAGGCC	7012	7031	461265	461284	3564
1342041	CAGTCAATTCAATACTCGAA	6016	6035	460269	460288	3565
1342042	GTCCATAGTCATGAACTATA	4427	4446	458680	458699	3566
1342043	ATAGCAGCTATTTCATGACT	N/A	N/A	439445	439464	3567
1342047	GTCAATTCAATACTCGAAGT	6014	6033	460267	460286	3568
1342048	GATCCAGTCAATTCAATACT	6020	6039	460273	460292	3569

1342049	TAACCAATCTATCACACCAA	N/A	N/A	444349	444368	3570
1342056	ATGACTCTTCACTCATGTTT	N/A	N/A	440233	440252	3571
1342058	GACTATTTTCAACTCAAGCT	N/A	N/A	439429	439448	3572
1342059	CTTGGTGGTCATTTATTGTC	4768	4787	459021	459040	3573
1342061	GGTGGTCATTTATTGTCACA	4765	4784	459018	459037	3574
1342062	TAGTTGCAGCCATCCAAGTA	5482	5501	459735	459754	3575
1342064	TGGTGGTCATTTATTGTCAC	4766	4785	459019	459038	3576
1342067	GTTCAGTTTAGTTGCAGCCA	5490	5509	459743	459762	3577
1342071	CATACTAGTTCATAATTCAC	4747	4766	459000	459019	3578
1342072	TCGCCCTGACTAATTTCTTG	7044	7063	461297	461316	3579
1342073	CCCTGACTAATTTCTTGGTG	7041	7060	461294	461313	3580
1342077	GCCCTGACTAATTTCTTGGT	7042	7061	461295	461314	3581

The compounds in table 54 are 5-10-5 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides, the 5' wing segment consists of five 2'-MOE nucleosides, and the 3' wing segment consists of five 2'-MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeeddddddddddeeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sssosssssssssssosss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 54

5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1364280	ACCCGAGTTGTCCATAGTCA	4436	4455	458689	458708	582
1364281	CCACGCTTTTATTTTCTGAT	N/A	N/A	439093	439112	2074
1364282	GCCTTTATAACTTTTCTTTC	N/A	N/A	446680	446699	2552
1364283	GGTCATTTATTGTCACATAC	4762	4781	459015	459034	194
1364285	ATTTTCTTTTTTCTGTGCCT	N/A	N/A	452653	452672	488
1367569	TTCCTCTTACCATCAAAGGC	5906	5925	460159	460178	2502
1367572	CGTGGGTGTTCGCTCTCTCC	4256	4275	458509	458528	3582
1367573	GCGTGGGTGTTCGCTCTCTC	4257	4276	458510	458529	3583
1367575	CTCTTACCATCAAAGGCTAA	5903	5922	460156	460175	3584
1367576	CCTCTTACCATCAAAGGCTA	5904	5923	460157	460176	2425
1367577	TCCTCTTACCATCAAAGGCT	5905	5924	460158	460177	431
1367580	CAGCCCGTATTCCTCTTACC	5915	5934	460168	460187	509
1367581	TGTGGCAGCCCGTATTCCTC	5920	5939	460173	460192	3585
1367586	GGGTGTTCGCTCTCTCCCTC	4253	4272	458506	458525	3586
1367588	GTGGGTGTTCGCTCTCTCCC	4255	4274	458508	458527	3587
1367589	CCGTATTCCTCTTACCATCA	5911	5930	460164	460183	3588
1367590	GTATTCCTCTTACCATCAAA	5909	5928	460162	460181	3589

1367591	CCCGTATTCCTCTTACCATC	5912	5931	460165	460184	3590
1394153	CCCGAGTTGTCCATAGTCAT	4435	4454	458688	458707	3563
1394154	GCACCCGAGTTGTCCATAGT	4438	4457	458691	458710	3605
1394155	CACCCGAGTTGTCCATAGTC	4437	4456	458690	458709	3593
1394156	GTCAGGTATTTGTTCAGTTT	5501	5520	459754	459773	3402
1394157	TGTTCAGTTTAGTTGCAGCC	5491	5510	459744	459763	274
1394158	TTGTTCAGTTTAGTTGCAGC	5492	5511	459745	459764	3655
1394159	GTTCAGTTTAGTTGCAGCCA	5490	5509	459743	459762	3577
1394160	TCAGGTATTTGTTCAGTTTA	5500	5519	459753	459772	3331
1394161	GCCCGTATTCCTCTTACCAT	5913	5932	460166	460185	2579
1394507	GGTGGTCATTTATTGTCACA	4765	4784	459018	459037	3574
1394508	GTGATTGTGTTCCATTGTAA	7024	7043	461277	461296	201
1394510	CCTTGCACTTTTGTTTCTAC	N/A	N/A	441090	441109	321
1394511	GTGGTCATTTATTGTCACAT	4764	4783	459017	459036	3560
1394512	ATGTGTTCTTAAATTCTCTA	8210	8229	462463	462482	1583
1394513	GCACGGTATTAGTGTCTTCA	7892	7911	462145	462164	126
1394514	GCTTCTCAAATCAGGTGTAC	8481	8500	462734	462753	1045
1394515	TGATTGTGTTCCATTGTAAA	7023	7042	461276	461295	3533
1394516	GTTTGTTGGTTTCTTATTAA	7083	7102	461336	461355	46
1394517	CTGTATATTTATTACTTGAT	8228	8247	462481	462500	1891
1394518	TGGTCATTTATTGTCACATA	4763	4782	459016	459035	3038

The compounds in table 55 are 6-10-4 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides, the 5' wing segment consists of six 2'-MOE nucleosides, and the 3' wing segment consists of four 2'-MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeeddddddddddeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sooooossssssssssoss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 55

6-10-4 MOE gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1371806	GTTCGCTCTCTCCCTCTCCC	4249	4268	458502	458521	114
1371807	TTTTCTTTTCGCCCTGACTA	7052	7071	461305	461324	3591
1371808	TCATTTATTGTCACATACTA	4760	4779	459013	459032	3592
1371809	CACCCGAGTTGTCCATAGTC	4437	4456	458690	458709	3593
1371810	GTCATTTATTGTCACATACT	4761	4780	459014	459033	3594
1371811	TTTTTTCTTTTCGCCCTGAC	7054	7073	461307	461326	3595
1371812	GTTGTCCATAGTCATGAACT	4430	4449	458683	458702	3596

1371813	TAATTCACATTCATCCCTTT	4735	4754	458988	459007	3597
1371814	CCCTGACTAATTTCTTGGTG	7041	7060	461294	461313	3580
1371815	ATAATTCACATTCATCCCTT	4736	4755	458989	459008	2268
1371816	TGGTCATTTATTGTCACATA	4763	4782	459016	459035	3038
1371817	TTGTCCATAGTCATGAACTA	4429	4448	458682	458701	2421
1371818	AGTTGCAGCCATCCAAGTAA	5481	5500	459734	459753	2655
1371819	GTTCATAATTCACATTCATC	4740	4759	458993	459012	2499
1371820	GCCCCCAAACCCATTTTCTT	N/A	N/A	452665	452684	1026
1371821	CAGCCATCCAAGTAAGAATA	5476	5495	459729	459748	3557
1371822	TTCATAATTCACATTCATCC	4739	4758	458992	459011	2422
1371823	GAGAACAAAGTCTATGTGGC	5934	5953	460187	460206	2733
1371824	CCCGAGTTGTCCATAGTCAT	4435	4454	458688	458707	3563
1371825	AGCCCGTATTCCTCTTACCA	5914	5933	460167	460186	2656
1371826	TCCTAACACTGCACAGAAAC	4279	4298	458532	458551	3598
1371827	TCAGGTATTTGTTCAGTTTA	5500	5519	459753	459772	3331
1371828	TCCATAGTCATGAACTATAA	4426	4445	458679	458698	3599
1371829	GTCAGGTATTTGTTCAGTTT	5501	5520	459754	459773	3402
1371830	GTGATTGTGTTCCATTGTAA	7024	7043	461277	461296	201
1371831	CCATAGTCATGAACTATAAA	4425	4444	458678	458697	3600
1371832	TTTTTCTGTGCCTCCTGACC	N/A	N/A	452646	452665	795
1371833	TGATTGTGTTCCATTGTAAA	7023	7042	461276	461295	3533
1371834	CCTGACTAATTTCTTGGTGA	7040	7059	461293	461312	2350
1371835	CATAGTCATGAACTATAAAC	4424	4443	458677	458696	3601
1371836	GAGTTGTCCATAGTCATGAA	4432	4451	458685	458704	3534
1371837	AAAGAAAAGTCAGGTATTTG	5509	5528	459762	459781	3332
1371838	GCCCTGACTAATTTCTTGGT	7042	7061	461295	461314	3581
1371839	ACAGAAACCAGCGTGGGTGT	4267	4286	458520	458539	3602
1371840	CTGACTAATTTCTTGGTGAT	7039	7058	461292	461311	3559
1371841	CCTCTTACCATCAAAGGCTA	5904	5923	460157	460176	2425
1371842	GCCCGTATTCCTCTTACCAT	5913	5932	460166	460185	2579
1371843	GCAGCCATCCAAGTAAGAAT	5477	5496	459730	459749	2578
1371844	TCATAATTCACATTCATCCC	4738	4757	458991	459010	2345
1371845	AGTTCATAATTCACATTCAT	4741	4760	458994	459013	2576
1371846	GTGTTCCATTGTAAACGCAA	7018	7037	461271	461290	123
1371847	ATTTTCTTTTTTCTGTGCCT	N/A	N/A	452653	452672	488
1371848	GGTCATTTATTGTCACATAC	4762	4781	459015	459034	194
1371849	TCCTCTTACCATCAAAGGCT	5905	5924	460158	460177	431
1371850	TGGGTGTTCGCTCTCTCCCT	4254	4273	458507	458526	270
1371851	ACCCGAGTTGTCCATAGTCA	4436	4455	458689	458708	582
1371852	CTGCACAGAAACCAGCGTGG	4271	4290	458524	458543	3603
1371853	CATAATTCACATTCATCCCT	4737	4756	458990	459009	3604
1371854	GCACCCGAGTTGTCCATAGT	4438	4457	458691	458710	3605
1371855	TTTTTCTTTTCGCCCTGACT	7053	7072	461306	461325	3606

1371856	ACTGCACAGAAACCAGCGTG	4272	4291	458525	458544	3607
1371857	TGTGTTCCATTGTAAACGCA	7019	7038	461272	461291	3608
1371858	CCTAACACTGCACAGAAACC	4278	4297	458531	458550	3609
1371859	TTTTATCCCAGTCATTGGCC	N/A	N/A	452682	452701	3610
1371860	CCAGTCATTGGCCCCCAAAC	N/A	N/A	452675	452694	3611
1371861	GGGTGTTCGCTCTCTCCCTC	4253	4272	458506	458525	3586
1371862	TTTTCTGTGCCTCCTGACCT	N/A	N/A	452645	452664	3612
1371863	GACCTCTACCCTTGTGAGCA	N/A	N/A	452630	452649	3613
1371864	CACTGCACAGAAACCAGCGT	4273	4292	458526	458545	3614
1371865	TTAATGAGAACAAAGTCTAT	5939	5958	460192	460211	3615
1371866	CATCCAAGTAAGAATATTTA	5472	5491	459725	459744	3616
1371867	AACACTGCACAGAAACCAGC	4275	4294	458528	458547	3617
1371868	AATGAGAACAAAGTCTATGT	5937	5956	460190	460209	3618
1371869	GCCATCCAAGTAAGAATATT	5474	5493	459727	459746	3619
1371870	TGTGGCAGCCCGTATTCCTC	5920	5939	460173	460192	3585
1371871	GTTGCAGCCATCCAAGTAAG	5480	5499	459733	459752	3620
1371872	CCGAGTTGTCCATAGTCATG	4434	4453	458687	458706	3621
1371873	CAAAGTCTATGTGGCAGCCC	5929	5948	460182	460201	3622
1371874	TAACACTGCACAGAAACCAG	4276	4295	458529	458548	3623
1371875	CCCGTATTCCTCTTACCATC	5912	5931	460165	460184	3590
1371876	CAGTTTAGTTGCAGCCATCC	5487	5506	459740	459759	3624
1371877	GTATTCCTCTTACCATCAAA	5909	5928	460162	460181	3589
1394164	TGTTCAGTTTAGTTGCAGCC	5491	5510	459744	459763	274
1394165	CCGTATTCCTCTTACCATCA	5911	5930	460164	460183	3588
1394166	TTCAGTTTAGTTGCAGCCAT	5489	5508	459742	459761	3190
1394167	TTGTTCAGTTTAGTTGCAGC	5492	5511	459745	459764	3655
1394168	GTTCAGTTTAGTTGCAGCCA	5490	5509	459743	459762	3577
1394522	GCCTTTATAACTTTTCTTTC	N/A	N/A	446680	446699	2552
1394523	GGTGGTCATTTATTGTCACA	4765	4784	459018	459037	3574
1394524	CAGCCCGTATTCCTCTTACC	5915	5934	460168	460187	509
1394525	GCTTCTCAAATCAGGTGTAC	8481	8500	462734	462753	1045
1394526	CCACGCTTTTATTTTCTGAT	N/A	N/A	439093	439112	2074
1394527	GTGGTCATTTATTGTCACAT	4764	4783	459017	459036	3560
1394528	ATGTGTTCTTAAATTCTCTA	8210	8229	462463	462482	1583
1394529	GCACGGTATTAGTGTCTTCA	7892	7911	462145	462164	126
1394530	GTTTGTTGGTTTCTTATTAA	7083	7102	461336	461355	46
1394531	CTGTATATTTATTACTTGAT	8228	8247	462481	462500	1891
1394532	CCTTGCACTTTTGTTTCTAC	N/A	N/A	441090	441109	321

The compounds in table 56 are 5-8-4 mixed MOE/cEt gapmers with mixed internucleoside linkages. The gapmers are 17 nucleosides in length, wherein the central gap segment consists of eight 2'-β-D-deoxynucleosides, the 5' wing segment consists of five 2'-MOE nucleosides, and the 3' wing segment consists of two cEt nucleosides and two 2'-

MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeeddddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'k' represents a cEt sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sssosssssssssoss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 56

5-8-4 MOE/cEt mixed wing gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1365254	CACGCTTTTATTTTCTG	N/A	N/A	439095	439111	3625
1365255	CCACGCTTTTATTTTCT	N/A	N/A	439096	439112	3626
1365258	TTTATAACTTTTCTTTC	N/A	N/A	446680	446696	3627
1365259	CTTTATAACTTTTCTTT	N/A	N/A	446681	446697	3628
1365260	CCTTTATAACTTTTCTT	N/A	N/A	446682	446698	3629
1365261	GCCTTTATAACTTTTCT	N/A	N/A	446683	446699	3630
1365262	TCATTTATTGTCACATA	4763	4779	459016	459032	3631
1365263	CATTTATTGTCACATAC	4762	4778	459015	459031	3632
1365264	GTCATTTATTGTCACAT	4764	4780	459017	459033	3633
1365265	GGTCATTTATTGTCACA	4765	4781	459018	459034	3634
1365267	CCGAGTTGTCCATAGTC	4437	4453	458690	458706	3635
1365268	CCCGAGTTGTCCATAGT	4438	4454	458691	458707	3636
1365270	ACCCGAGTTGTCCATAG	4439	4455	458692	458708	3637
1365271	TCAGTTTAGTTGCAGCC	5491	5507	459744	459760	3638
1365272	CAGTTTAGTTGCAGCCA	5490	5506	459743	459759	3639
1365274	TTCAGTTTAGTTGCAGC	5492	5508	459745	459761	3640
1365275	TTCTTTTTTCTGTGCCT	N/A	N/A	452653	452669	3641

The compounds in table 57 are 5-8-4 mixed gapmers with mixed internucleoside linkages. The mixed gapmers have mixed cEt/MOE wings and a 2'-OMe modified nucleoside at position 2 of the gap. The gapmers are 17 nucleosides in length, wherein the 5' wing segment consists of five 2'-MOE nucleosides, the 3' wing segment consists of two cEt nucleosides and two 2'-MOE nucleosides. The gap is eight nucleosides in length, and has a nucleoside comprising a 2'-β-D-deoxyribosyl sugar moiety at positions 1, 3, 4, 5, 6, 7, and 8 of the gap (counting from the 5' end) and 2'-OMe nucleoside at position 2 of the gap (counting from the 5' end). The sugar motif of the mixed gapmers is (from 5' to 3'): eeeeedyddddddkkee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, 'y' represents a 2'-O-methyl ribose sugar moiety, 'k' represents a cEt sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sssosssssssssoss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 57

5-8-4 MOE/cEt mixed gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1365278	CGCTTTUATTTTCTGAT	N/A	N/A	439093	439109	3642
1365281	CCACGCUTTTATTTTCT	N/A	N/A	439096	439112	3643
1365282	TTTATAACTTTTCTTTC	N/A	N/A	446680	446696	3627
1365283	CCTTTAUAACTTTTCTT	N/A	N/A	446682	446698	3644
1365284	GCCTTTATAACTTTTCT	N/A	N/A	446683	446699	3630
1365285	CATTTAUTGTCACATAC	4762	4778	459015	459031	3645
1365286	TCATTTATTGTCACATA	4763	4779	459016	459032	3631
1365287	CTTTATAACTTTTCTTT	N/A	N/A	446681	446697	3628
1365288	GTCATTUATTGTCACAT	4764	4780	459017	459033	3646
1365289	GGTCATUTATTGTCACA	4765	4781	459018	459034	3647
1365290	CCGAGTUGTCCATAGTC	4437	4453	458690	458706	3648
1365291	CGAGTTGTCCATAGTCA	4436	4452	458689	458705	3649
1365292	ACCCGAGTTGTCCATAG	4439	4455	458692	458708	3637
1365293	TTTCTTUTTTCTGTGCC	N/A	N/A	452654	452670	3650
1365294	CAGTTTAGTTGCAGCCA	5490	5506	459743	459759	3639
1365297	TTCTTTUTTCTGTGCCT	N/A	N/A	452653	452669	3651
1365298	CCCGAGUTGTCCATAGT	4438	4454	458691	458707	3652
1365299	TTCAGTUTAGTTGCAGC	5492	5508	459745	459761	3653
1365300	TCAGTTUAGTTGCAGCC	5491	5507	459744	459760	3654

The compounds in table 58 are 5-8-4 MOE gapmers with mixed internucleoside linkages. The gapmers are 17 nucleosides in length, wherein the central gap segment consists of eight 2'-β-D-deoxynucleosides, the 5' wing segment consists of five 2'-MOE nucleosides, and the 3' wing segment consists of four 2'-MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeddddddddeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sssosssssssssoss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 58

5-8-4 MOE gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1385293	TCAGTTTAGTTGCAGCC	5491	5507	459744	459760	3638
1385294	GGTCATTTATTGTCACA	4765	4781	459018	459034	3634
1385295	CCGAGTTGTCCATAGTC	4437	4453	458690	458706	3635
1394533	CAGTTTAGTTGCAGCCA	5490	5506	459743	459759	3639

1394534	CGAGTTGTCCATAGTCA	4436	4452	458689	458705	3649
1394537	GCACCCGAGTTGTCCAT	4441	4457	458694	458710	3656
1394538	CAGCCCGTATTCCTCTT	5918	5934	460171	460187	3657
1394539	CACCCGAGTTGTCCATA	4440	4456	458693	458709	3658
1394540	GAGTTGTCCATAGTCAT	4435	4451	458688	458704	3659
1394541	CCCGTATTCCTCTTACC	5915	5931	460168	460184	3660
1394543	AGCCCGTATTCCTCTTA	5917	5933	460170	460186	3661
1394544	AGTTTAGTTGCAGCCAT	5489	5505	459742	459758	3662
1394545	GTATTCCTCTTACCATC	5912	5928	460165	460181	3663
1394546	TTCAGTTTAGTTGCAGC	5492	5508	459745	459761	3640
1394547	CCCGAGTTGTCCATAGT	4438	4454	458691	458707	3636
1394548	CGTATTCCTCTTACCAT	5913	5929	460166	460182	3664
1394549	TGTTCAGTTTAGTTGCA	5494	5510	459747	459763	3665
1394550	TATTCCTCTTACCATCA	5911	5927	460164	460180	3666
1394551	CCGTATTCCTCTTACCA	5914	5930	460167	460183	3667
1394552	GCCCGTATTCCTCTTAC	5916	5932	460169	460185	3668
1394553	TTGTTCAGTTTAGTTGC	5495	5511	459748	459764	3669

The compounds in table 59 are 5-10-5 MOE gapmers with mixed internucleoside linkages. The gapmers are 20 nucleosides in length, wherein the central gap segment consists of ten 2'-β-D-deoxynucleosides, the 5' wing segment consists of five 2'-MOE nucleosides, and the 3' wing segment consists of five 2'-MOE nucleosides. The sugar motif of the gapmers is (from 5' to 3'): eeeeeddddddddddeeeee; wherein 'd' represents a 2'-β-D-deoxyribosyl sugar moiety, and 'e' represents a 2'-MOE sugar moiety. The gapmers have an internucleoside linkage motif of (from 5' to 3'): sooossssssssssssooss; wherein "s" represents a phosphorothioate internucleoside linkage and "o" represents a phosphodiester internucleoside linkage. All cytosine residues are 5-methylcytosines.

Table 59

5-10-5 MOE gapmers with mixed PO/PS internucleoside linkages complementary to human ATXN1

Compound Number	SEQUENCE	SEQ ID No: 1 Start Site	SEQ ID No: 1 Stop Site	SEQ ID No: 2 Start Site	SEQ ID No: 2 Stop Site	SEQ ID No.
1371311	CCCGTATTCCTCTTACCATC	5912	5931	460165	460184	3590
1371320	TGTGGCAGCCCGTATTCCTC	5920	5939	460173	460192	3585
1371322	CACCCGAGTTGTCCATAGTC	4437	4456	458690	458709	3593
1371325	GCACCCGAGTTGTCCATAGT	4438	4457	458691	458710	3605
1394162	TTGTTCAGTTTAGTTGCAGC	5492	5511	459745	459764	3655
1394163	CCGTATTCCTCTTACCATCA	5911	5930	460164	460183	3588

Example 5: Tolerability of modified oligonucleotides complementary to human ATXN1 in rats, long-term assessment

In separate studies run under the same conditions, modified oligonucleotides described above were tested in Sprague Dawley rats to assess the long-term tolerability of the oligonucleotides. Sprague Dawley rats each received a single intrathecal (IT) delivered dose of 3mg of oligonucleotide or PBS. Each animal was weighed and evaluated weekly by a trained observer for adverse events. Adverse events were defined as neurological dysfunction not typical in

PBS-treated control animals, including, but not limited to: abnormal limb splay, abnormal gait, tremors, abnormal respiration, paralysis, and spasticity. Animals treated with Compound No. 994509, Compound No. 1040500, Compound No. 1041927, Compound No. 1055001, Compound No. 1371311, or Compound No. 1385293 achieved no adverse events for the duration of the study.

Example 6: Activity of modified oligonucleotides complementary to human ATXN1 in transgenic mice

A transgenic mouse model was developed in the laboratories of Drs. Harry Orr and Michael Koob at the University of Minnesota. The construct contains human Atxn1 exon 8, intron 8 and exon 9 including the entire 3' UTR (Banfi et al. Nat. Genet. 7: 513-520, 1994) (including nucleosides 435531-464889 of SEQ ID NO:2) flanked by Frt sites for FLP recombinase and the selection marker Hygro flanked by LoxN sites for CRE recombinase. The construct was injected into mouse blastocysts. The human sequence of exon 8, intron 8 and exon 9 replace the mouse Atxn1 exon 7, intron 7, and exon 8. The Hygro cassette was removed via recombination to generate chimeric mice expressing human coding sequence exon 8 and exon 9. Human RNA expression is found in brain and spinal cord in this model. There is a one base deletion causing a stop codon at amino acid 190, so protein is not generated.

Transgenic mice described above were used to test activity of modified oligonucleotides described above.

Treatment

ATXN1 transgenic mice were treated with a single ICV bolus of 300 μg of modified oligonucleotide. A group of 3-4 mice received PBS as a negative control on each treatment day, and the PCR values were normalized to the PBS control group for mice treated on the same day. In some cases, individual mice treated with a given modified oligonucleotide were treated on different days, and the reported results for each modified oligonucleotide in the table below represent the average across 1-3 independent experiments representing 1-5 treated mice for each modified oligonucleotide.

RNA analysis

Two weeks post treatment, mice were sacrificed, and RNA was extracted from cortical brain tissue for real-time qPCR analysis of RNA expression of ATXN1 using primer probe set RTS37573 (described herein above). Results are presented as percent change of RNA, relative to PBS control, normalized to mouse cyclophilin A. Data indicated as "n.d." (no data) means that no data are available for that tissue for that compound.

As shown in the table below, treatment with modified oligonucleotides resulted in reduction of ATXN1 RNA in comparison to the PBS control.

Table 60

Reduction of human ATXN1 RNA in transgenic mice

Compound Number	ATXN1 RNA (%control)
994334	88
994341	80
994346	74

994351	51
994366	99
994367	83
994374	82
994375	88
994398	30
994408	72
994409	80
994413	18
994417	95
994418	54
994419	28
994421	15
994424	62
994429	63
994430	36
994434	63
994437	22
994442	76
994443	62
994447	52
994448	62
994449	58
994453	58
994458	24
994459	36
994460	50
994464	49
994465	65
994467	59
994468	43
994469	32
994484	50
994485	90
994486	37
994491	51
994492	37
994493	19
994494	26
994495	48
994501	69
994502	67
994503	63

994506	56
994507	73
994508	81
994509	33
994517	89
994518	45
994520	48
994522	55
994526	36
994527	38
994539	63
994540	44
994541	82
994543	91
994545	59
994559	84
994561	65
994562	57
994564	73
994567	81
994569	46
994571	75
994809	57
994810	50
994811	43
994813	66
994819	46
994823	42
994829	86
994831	91
994836	94
994840	71
994841	67
994854	89
994856	72
994857	73
994859	78
994874	88
994876	81
994877	42
994878	92
994885	61
994887	71

994895	52
994904	33
994906	68
994913	18
994921	51
994925	91
1040083	83
1040084	39
1040085	48
1040092	62
1040107	104
1040109	59
1040146	55
1040151	64
1040170	56
1040173	94
1040180	93
1040191	108
1040198	107
1040199	69
1040203	75
1040207	75
1040213	85
1040223	60
1040227	80
1040231	56
1040236	91
1040237	59
1040238	79
1040239	72
1040248	82
1040297	63
1040299	48
1040328	17
1040329	32
1040334	84
1040335	90
1040337	51
1040338	66
1040389	92
1040413	81
1040435	81
1040438	75

1040442	85
1040472	93
1040475	44
1040479	27
1040500	38
1040502	84
1040512	49
1040514	74
1040597	92
1040601	72
1041318	49
1041319	88
1041326	82
1041328	51
1041334	90
1041339	90
1041345	87
1041355	63
1041366	71
1041390	41
1041398	48
1041400	72
1041406	98
1041409	37
1041413	62
1041425	69
1041429	65
1041433	73
1041434	103
1041438	85
1041439	66
1041441	86
1041443	101
1041455	77
1041469	75
1041471	48
1041486	48
1041489	101
1041498	43
1041527	95
1041532	85
1041537	87
1041548	98

1041550	114
1041557	83
1041567	71
1041575	103
1041597	119
1041603	96
1041605	82
1041608	76
1041623	64
1041636	70
1041649	94
1041653	84
1041676	91
1041679	88
1041682	103
1041699	75
1041729	79
1041733	113
1041736	72
1041746	42
1041757	66
1041768	63
1041769	47
1041776	99
1041777	86
1041927	37
1042257	105
1042471	60
1055001	27
1055004	34
1055006	46
1055007	34
1055012	63
1055013	76
1055014	50
1055017	92
1055020	71
1055025	95
1055027	73
1055035	68
1055046	98
1055050	73
1342029	49

1342030	107
1342031	80
1342032	48
1342033	77
1342034	92
1342035	89
1342036	60
1342037	89
1342038	63
1342039	86
1342040	117
1342041	58
1342042	80
1342043	95
1342044	78
1342045	101
1342046	83
1342047	86
1342048	64
1342049	88
1342050	107
1342051	80
1342052	98
1342053	87
1342054	106
1342055	97
1342056	86
1342057	99
1342058	55
1342059	97
1342060	107
1342061	86
1342062	73
1342063	68
1342064	68
1342065	76
1342066	98
1342067	25
1342068	58
1342069	83
1342070	94
1342071	88
1342072	82

1342073	77
1342074	74
1342075	43
1342076	86
1342077	69
1364280	36
1364281	48
1364282	41
1364283	26
1364285	29
1365254	65
1365255	62
1365258	123
1365259	121
1365260	94
1365261	49
1365262	76
1365263	69
1365264	43
1365265	34
1365267	44
1365268	44
1365270	49
1365271	28
1365272	38
1365274	46
1365275	51
1365278	81
1365281	71
1365282	92
1365283	83
1365284	92
1365285	76
1365286	79
1365287	61
1365288	71
1365289	72
1365290	69
1365291	55
1365292	45
1365293	94
1365294	65
1365297	96

1365298	53
1365299	75
1365300	51
1367569	80
1367572	53
1367573	44
1367575	99
1367576	89
1367577	52
1367580	46
1367581	42
1367586	66
1367588	59
1367589	19
1367590	80
1367591	21
1371311	24
1371320	66
1371322	79
1371325	48
1371806	52
1371807	70
1371808	78
1371809	62
1371810	50
1371811	74
1371812	89
1371813	112
1371814	70
1371815	76
1371816	51
1371817	62
1371818	35
1371819	49
1371820	68
1371821	62
1371822	60
1371823	90
1371824	60
1371825	29
1371826	70
1371827	59
1371828	63

1371829	32
1371830	60
1371831	86
1371832	84
1371833	81
1371834	89
1371835	92
1371836	111
1371837	96
1371838	90
1371839	81
1371840	87
1371841	83
1371842	29
1371843	71
1371844	59
1371845	73
1371846	62
1371847	82
1371848	38
1371849	72
1371850	78
1371851	49
1371852	89
1371853	66
1371854	37
1371855	36
1371856	77
1371857	76
1371858	104
1371859	94
1371860	98
1371861	86
1371862	75
1371863	68
1371864	81
1371865	87
1371866	58
1371867	83
1371868	85
1371869	70
1371870	46
1371871	60

1371872	56
1371873	78
1371874	77
1371875	17
1371876	39
1371877	48
1385293	31
1385294	25
1385295	27
1394153	41
1394154	65
1394155	49
1394156	40
1394157	30
1394158	33
1394159	24
1394160	30
1394161	29
1394162	45
1394163	35
1394164	42
1394165	43
1394166	43
1394167	28
1394168	33
1394507	46
1394508	63
1394510	66
1394511	77
1394512	54
1394513	38
1394514	73
1394515	87
1394516	72
1394517	91
1394518	73
1394522	40
1394523	86
1394524	32
1394525	43
1394526	8
1394527	68
1394528	71

1394529	38
1394530	38
1394531	65
1394532	42
1394533	38
1394534	66
1394537	45
1394538	54
1394539	58
1394540	59
1394541	67
1394543	46
1394544	43
1394545	66
1394546	26
1394547	53
1394548	88
1394549	51
1394550	92
1394551	48
1394552	33
1394553	85

Example 7: Activity of modified oligonucleotides complementary to human ATXN1 in transgenic mice, multiple doses

Modified oligonucleotides described above were tested in the ATXN1 transgenic mice described herein above.

Treatment

ATXN1 transgenic mice were divided into groups of 3-4 mice each. Each mouse received a single ICV bolus of modified oligonucleotide at the doses described in the tables below and were sacrificed two weeks later. A group of 4 mice received PBS as a negative control for each experiment. Each table represents a separate experiment.

RNA analysis

After two weeks, mice were sacrificed, and RNA was extracted from cortical brain tissue for real-time PCR analysis of measurement of RNA expression of ATXN1 using primer probe set RTS37573. Results are presented as percent change of RNA, relative to PBS control, normalized to mouse cyclophilin A (measured by primer-probe set m_cyclo24 described herein above). ED50 values were calculated in GraphPad Prism. N/A means that an ED50 value could not be reliably calculated for that experiment.

As shown in the tables below, treatment with modified oligonucleotides resulted in dose-dependent reduction of ATXN1 RNA in comparison to the PBS control.

Table 61

Dose-dependent percent reduction of human ATXN1 RNA in the cortex of transgenic mice

Compound ID	Dose (µg)	ATXN1 RNA (%control)	ED50 (µg)
1040479	10	97	669.1
	30	86	
	100	87	
	300	59	
	700	51	
1040500	10	87	126.2
	30	83	
	100	59	
	300	44	
	700	22	
1367591	10	80	40.59
	30	66	
	100	32	
	300	23	
	700	22	
1371311	10	76	36.11
	30	57	
	100	45	
	300	19	
	700	14	
1371875	10	70	30.41
	30	67	
	100	25	
	300	12	
	700	9	
1394161	10	71	36.04
	30	68	
	100	35	
	300	18	
	700	8	

5

Table 62

Dose-dependent percent reduction of human ATXN1 RNA in transgenic mice

Compound ID	Dose (µg)	Cortex	
		ATXN1 RNA (%control)	ED50 (µg)
1041409	10	94	277.3
	30	88	

	100	78	
	300	56	
	700	34	
1055001	10	91	144
	30	89	
	100	75	
	300	23	
	700	18	
1055007	10	104	156.9
	30	88	
	100	75	
	300	31	
	700	22	
1371827	10	92	87.95
	30	77	
	100	50	
	300	34	
	700	22	

Table 63

Dose-dependent percent reduction of human ATXN1 RNA in transgenic mice

Compound ID	Dose (µg)	Cortex	
		ATXN1 RNA (%control)	ED50 (µg)
994823	10	110	308.3
	30	96	
	100	72	
	300	64	
	700	32	
1385293	10	90	93.14
	30	75	
	100	63	
	300	25	
	700	15	

Table 64

Dose-dependent percent reduction of human ATXN1 RNA in transgenic mice

Compound ID	Dose (µg)	Cortex	
		ATXN1 RNA (%control)	ED50 (µg)
994492	10	78	72.25
	30	72	
	100	52	

	300	41	
	700	22	
994509	10	80	27.84
	30	53	
	100	30	
	300	20	
	700	17	

Table 65

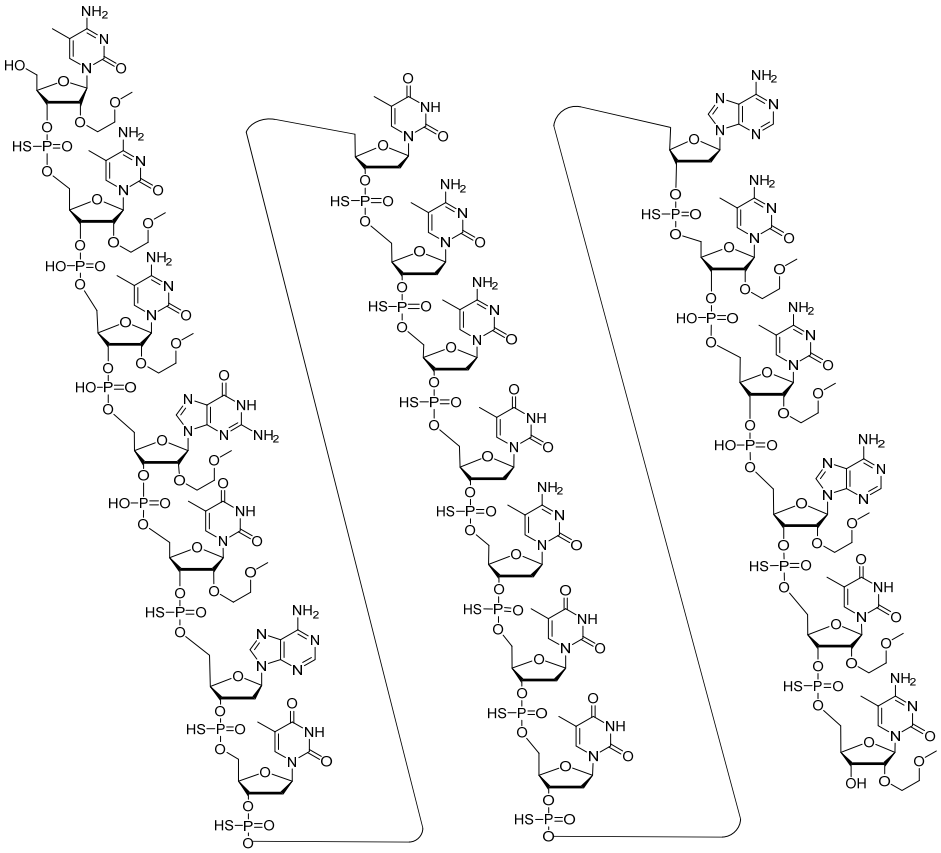
Dose-dependent percent reduction of human ATXN1 RNA in transgenic mice

Compound ID	Dose (µg)	Cortex	
		ATXN1 RNA (%control)	ED50 (µg)
1041927	10	72	52.22
	30	71	
	100	41	
	300	29	
	700	33	
994419	10	83	50.14
	30	65	
	100	46	
	300	22	
	700	17	
1394155	10	72	105.4
	30	70	
	100	60	
	300	41	
	700	40	

5

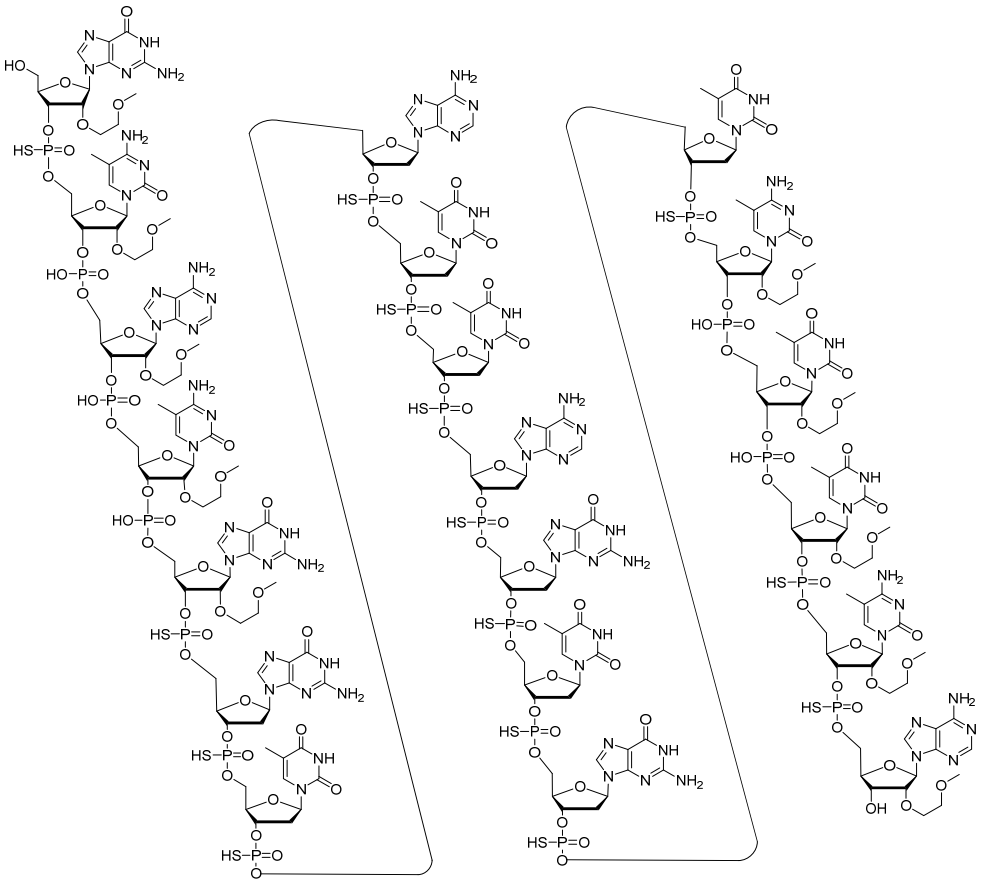
CLAIMS:

1. A modified oligonucleotide according to the following chemical structure:



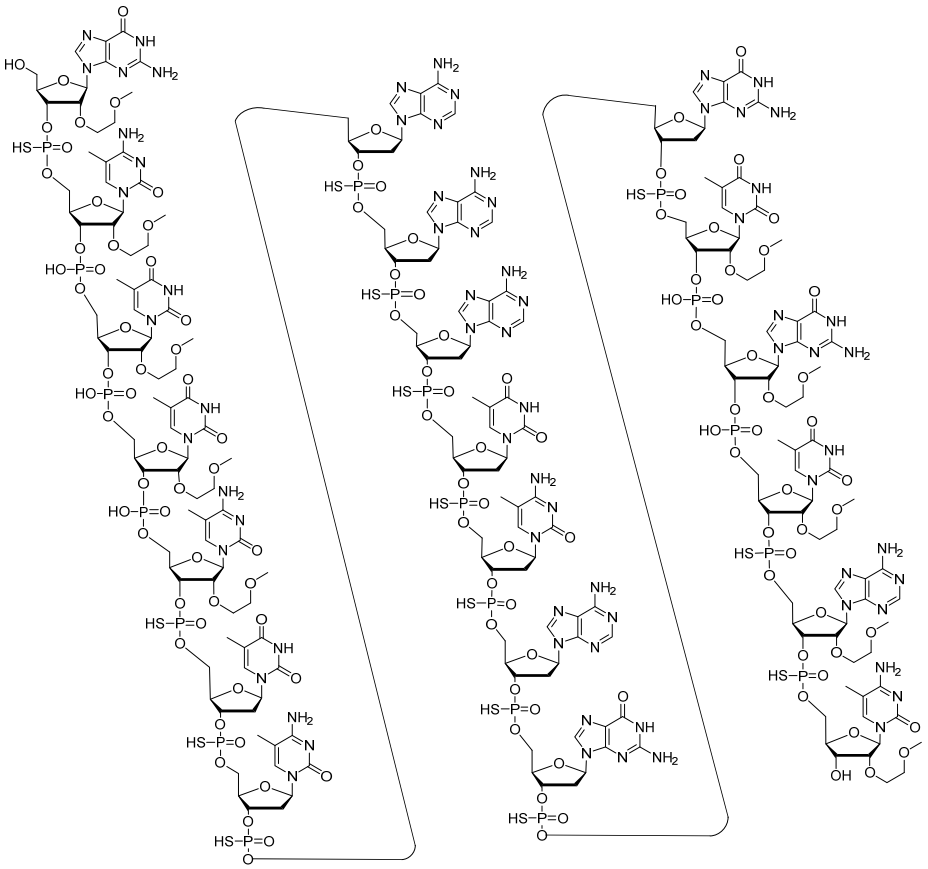
(SEQ ID NO: 3590), or a salt thereof.

2. A modified oligonucleotide according to the following chemical structure:



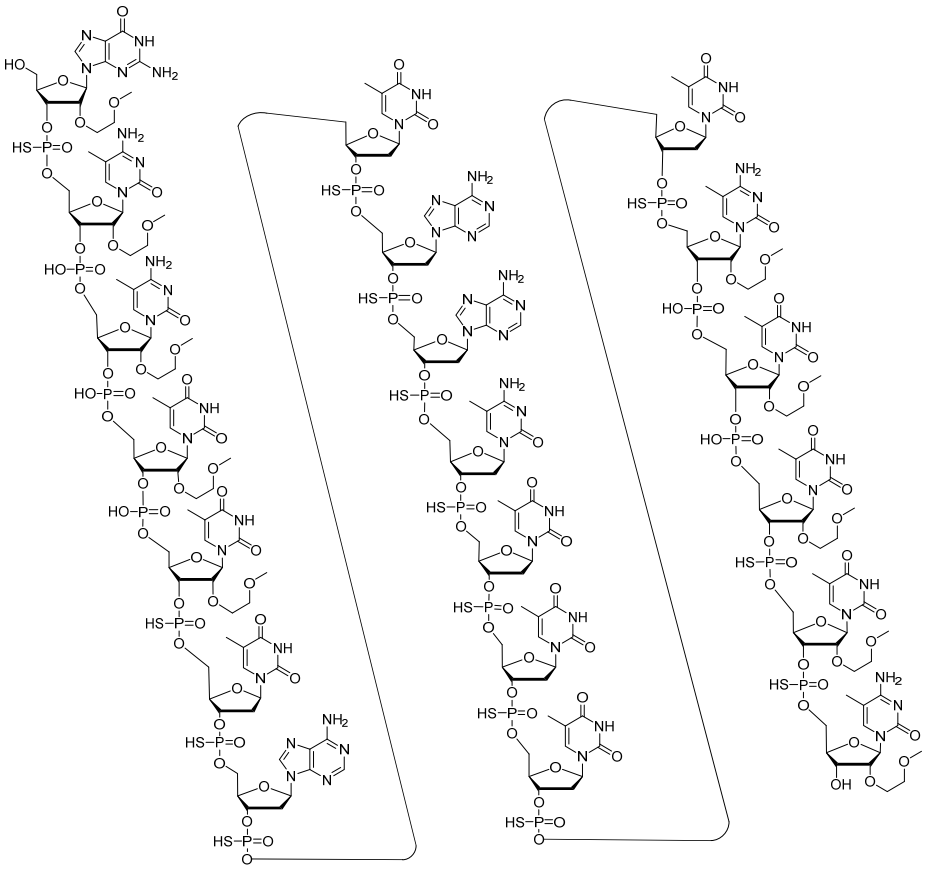
(SEQ ID NO: 126), or a salt thereof.

3. A modified oligonucleotide according to the following chemical structure:



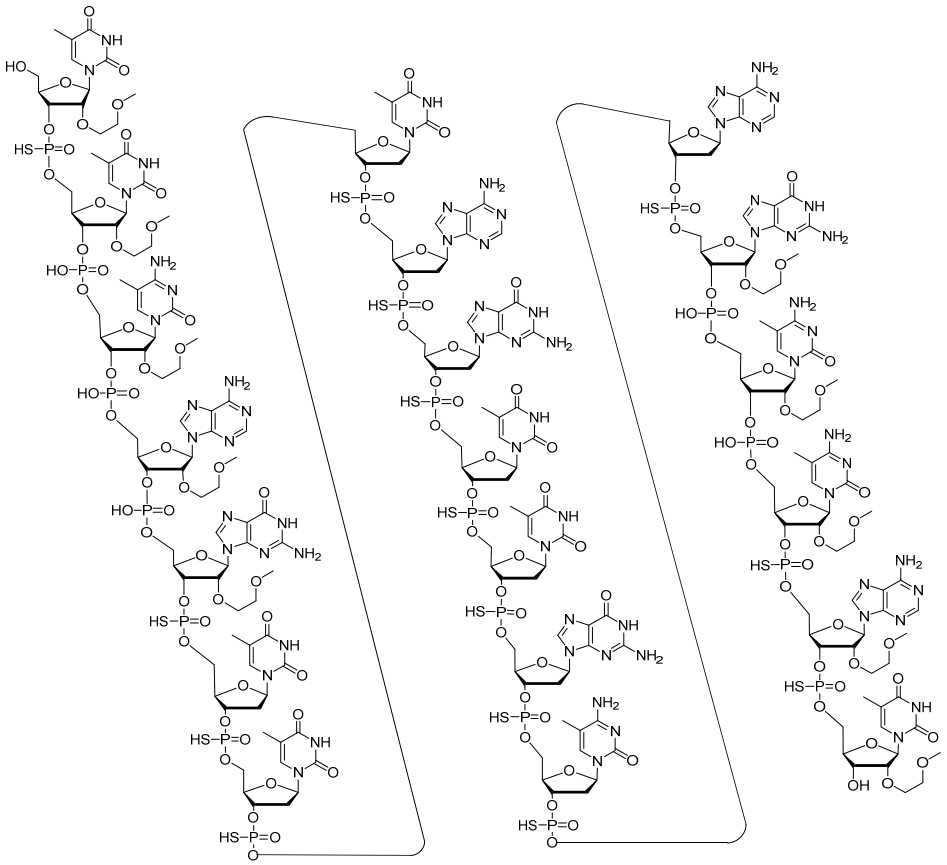
(SEQ ID NO: 1045), or a salt thereof.

4. A modified oligonucleotide according to the following chemical structure:



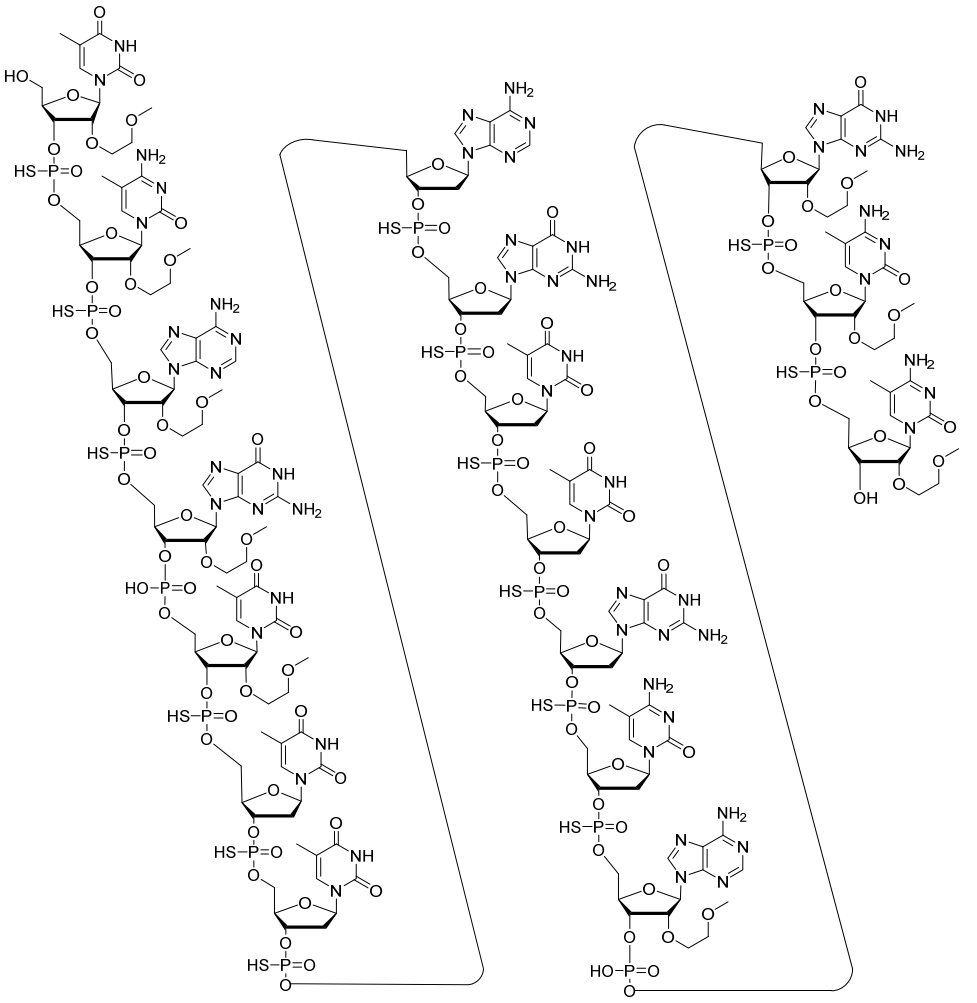
(SEQ ID NO: 2552), or a salt thereof.

5. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3190), or a salt thereof.

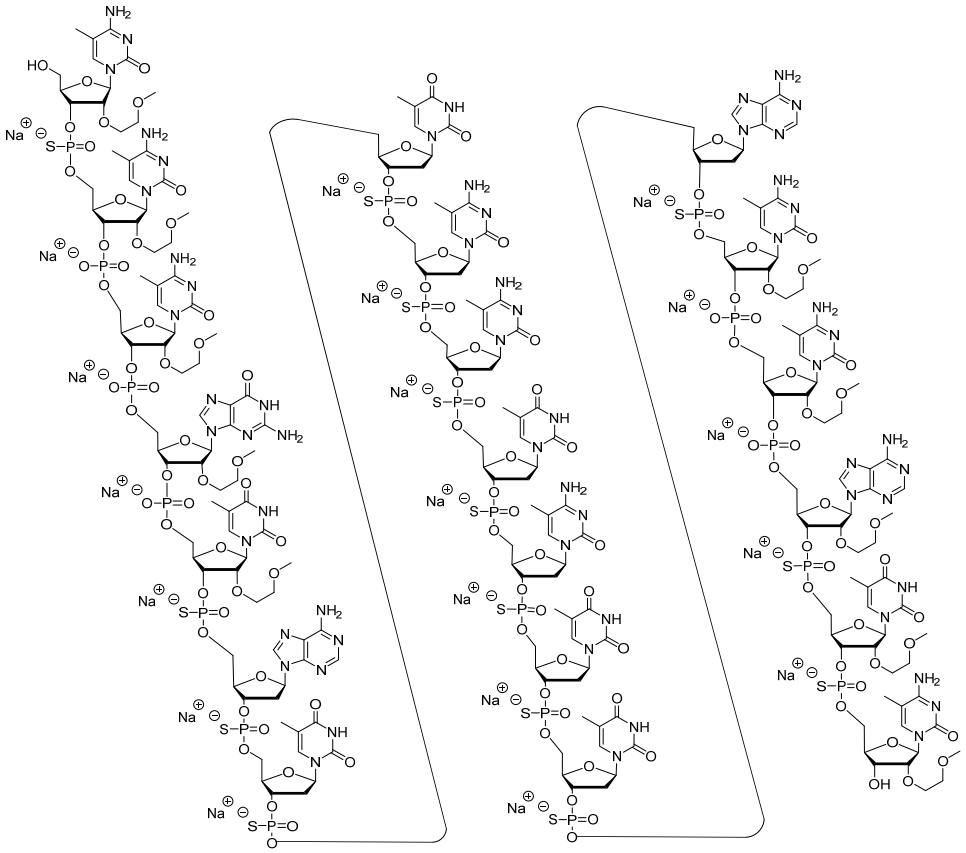
6. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3638), or a salt thereof.

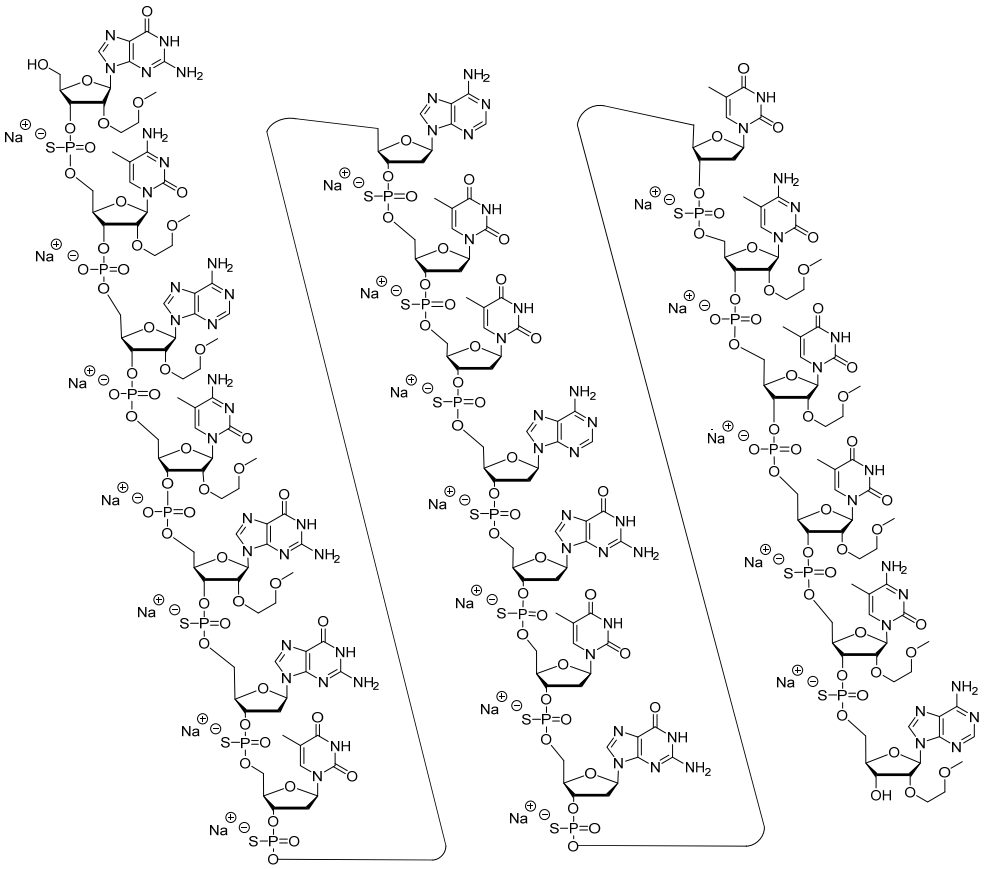
7. The modified oligonucleotide of any of claims 1-6, which is the sodium salt or the potassium salt.

8. A modified oligonucleotide according to the following chemical structure:



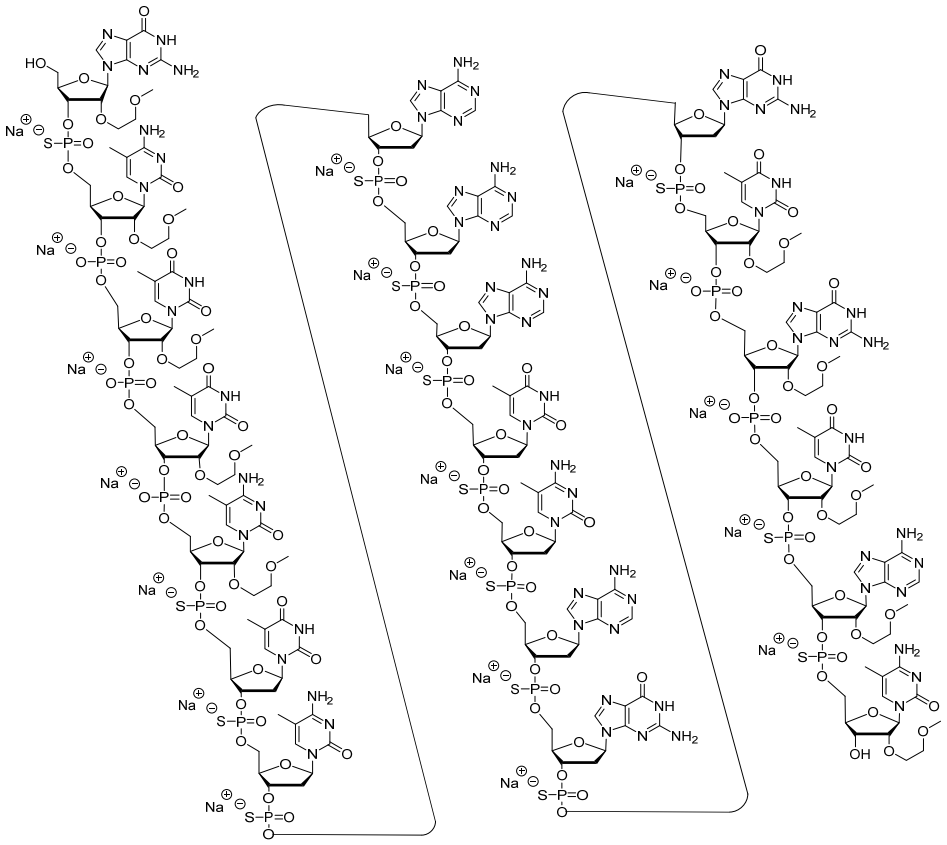
(SEQ ID NO: 3590).

9. A modified oligonucleotide according to the following chemical structure:



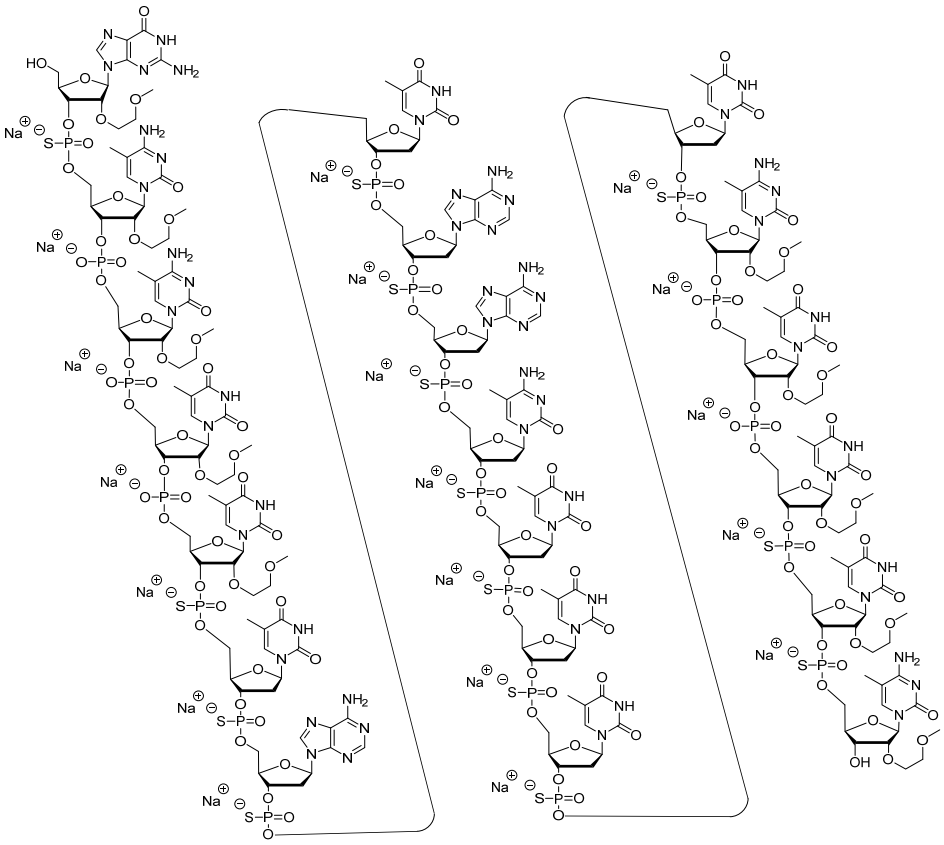
(SEQ ID NO: 126).

10. A modified oligonucleotide according to the following chemical structure:



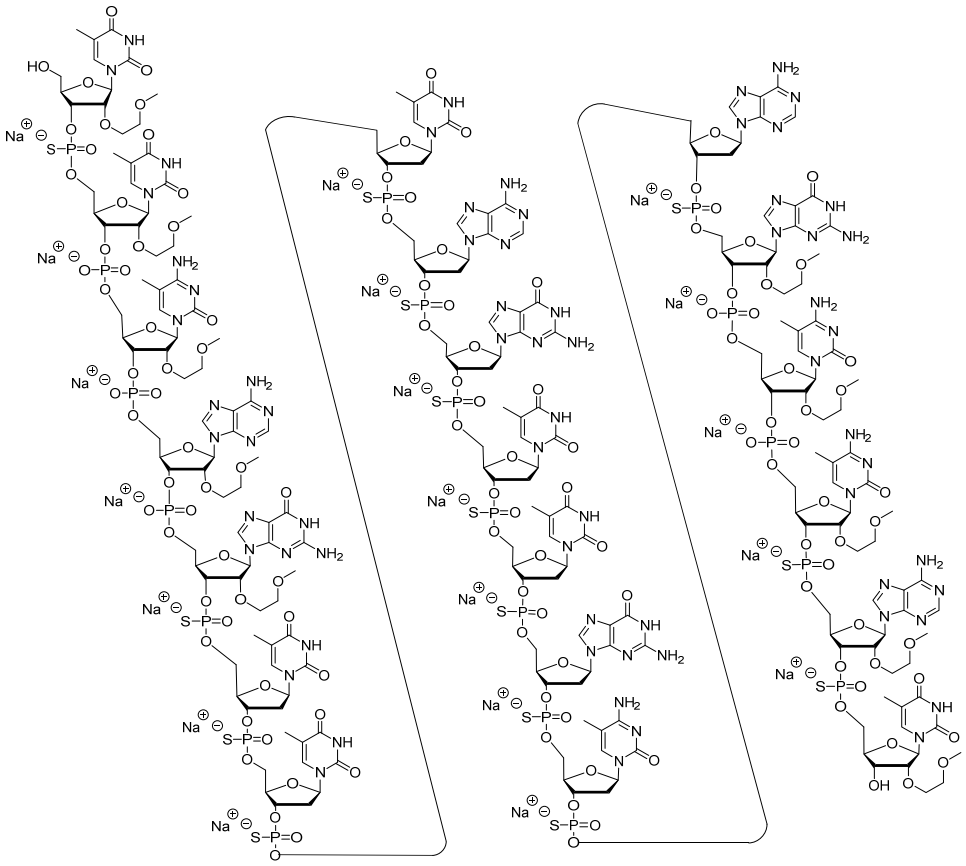
(SEQ ID NO: 1045).

11. A modified oligonucleotide according to the following chemical structure:



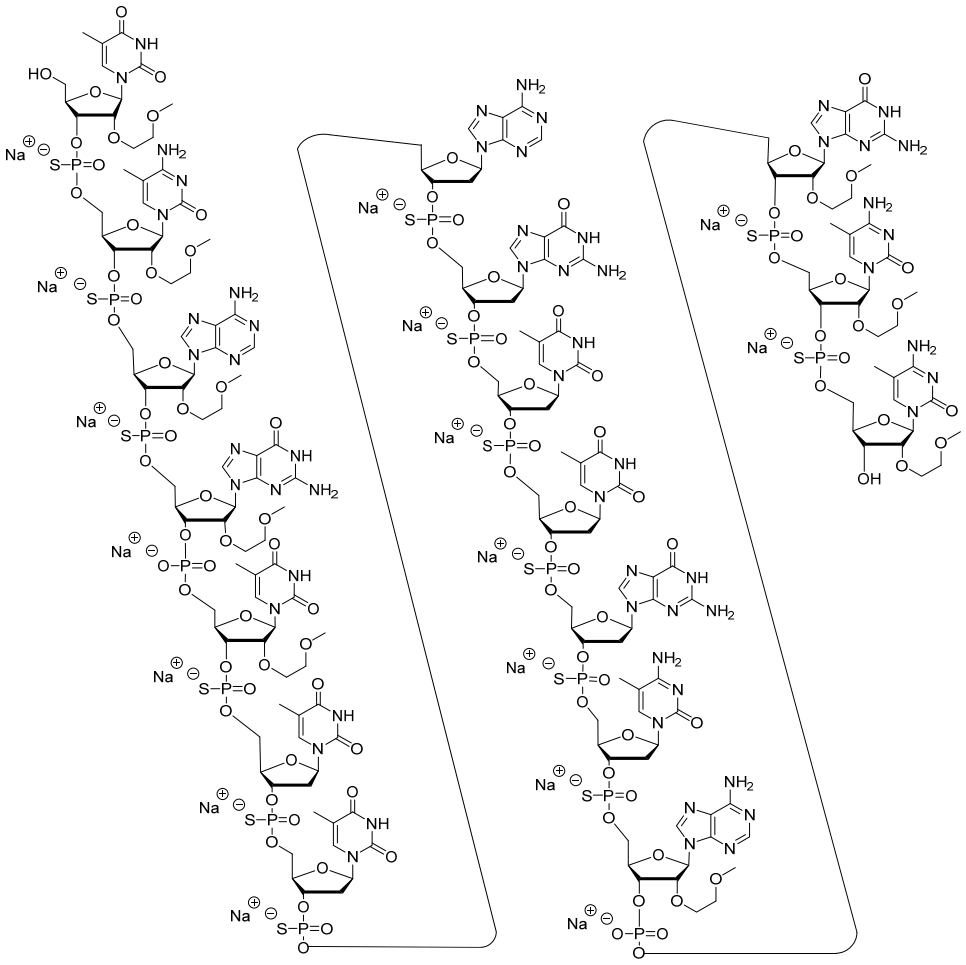
(SEQ ID NO: 2552).

12. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3190).

13. A modified oligonucleotide according to the following chemical structure:



(SEQ ID NO: 3638).

14. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: ^{m}Ces ^{m}Ceo ^{m}Ceo Geo Tes Ads Tds Tds ^{m}Cds ^{m}Cds Tds ^{m}Cds Tds Tds Ads ^{m}Ceo ^{m}Ceo Aes Tes ^{m}Ce (SEQ ID NO: 3590), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

15. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: Ges ^{m}Ceo Aeo ^{m}Ceo Ges Gds Tds Ads Tds Tds Ads Gds Tds Gds Tds ^{m}Ceo Teo Tes ^{m}Ces Ae (SEQ ID NO: 126), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

16. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: Ges ^{m}Ceo Teo Teo ^{m}Ces Tds ^{m}Cds Ads Ads Ads Tds ^{m}Cds Ads Gds Gds Teo Geo Tes Aes mCe (SEQ ID NO: 1045), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

17. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: Ges ^{m}Ceo ^{m}Ceo Teo Tes Tds Ads Tds Ads Ads ^{m}Cds Tds Tds Tds Tds ^{m}Ceo Teo Tes Tes ^{m}Ce (SEQ ID NO: 2552), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

18. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: Tes Teo ^{m}Ceo Aeo Ges Tds Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Ads Geo ^{m}Ceo ^{m}Ces Aes Te (SEQ ID NO: 3190), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

19. An oligomeric compound comprising a modified oligonucleotide according to the following chemical notation: Tes ^{m}Ces Aes Geo Tes Tds Tds Ads Gds Tds Tds Gds ^{m}Cds Aeo Ges ^{m}Ces ^{m}Ce (SEQ ID NO: 3638), wherein,

A = an adenine nucleobase,

^{m}C = a 5-methylcytosine nucleobase,

G = a guanine nucleobase,

T = a thymine nucleobase,

e = a 2'-MOE sugar moiety,

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

s = a phosphorothioate internucleoside linkage, and

o = a phosphodiester internucleoside linkage.

20. A population of modified oligonucleotides of any of claims 1-13, or a population of oligomeric compounds of any of claims 14-19, wherein all of the phosphorothioate internucleoside linkages of the modified oligonucleotides are stereorandom.

21. A pharmaceutical composition comprising the modified oligonucleotides of any of claims 1-13, the oligomeric compounds of any of claims 14-19, the population of modified oligonucleotides of claim 20, or the population of oligomeric compound of claim 20, and a pharmaceutically acceptable diluent.

22. The pharmaceutical composition of claim 21, wherein the pharmaceutically acceptable diluent is artificial cerebrospinal fluid or phosphate-buffered saline (PBS).

23. The pharmaceutical composition of claim 22, wherein the pharmaceutical composition:

a) consists essentially of the modified oligonucleotide or the oligomeric compound and artificial cerebrospinal fluid;

b) consists essentially of the modified oligonucleotide or the oligomeric compound and PBS;

c) consists essentially of the population of modified oligonucleotides or the population of oligomeric compounds and artificial cerebrospinal fluid; or

d) consists essentially of the population of modified oligonucleotides or the population of oligomeric compounds and PBS.