iRNA COMPOSITIONS AND METHODS FOR SILENCING GROWTH FACTOR RECEPTOR BOUND PROTEIN 14 (GRB14) IN THE LIVER

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of priority to U.S. Provisional Application No. 63/762,453, filed on February 24, 2025, and to U.S. Provisional Application No. 63/568,529, filed on March 22, 2024. The entire contents of the foregoing applications are hereby incorporated herein by reference.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been filed electronically in eXtensible Markup Language (XML) format and is hereby incorporated by reference in its entirety. Said XML copy, created on March 10, 2025, is named A108868_1630WO_SL.xml and is 55, 100, 878 bytes in size.

BACKGROUND OF THE DISCLOSURE

Insulin acts in the liver to increase uptake of glucose, decrease gluconeogenesis, and promote glycogen synthesis. Insulin promotes synthesis of carbohydrate (e.g., glycogen), fat (e.g., fatty acid, triacylglycerol, triglycerides), and protein in the muscle and adipose tissue. Insulin resistance increases risk of developing type 2 diabetes, non-alcoholic steatohepatitis (NASH), and other comorbidities including cardiovascular disease and cancer.

The prevalence of diabetes, e.g., type 2 diabetes, has progressively increased and is expected to continue increasing. The current treatment options for diabetes include lifestyle modifications, oral medications, insulin injections, and managing the associated comorbidities (*e.g.*, hypertension, hyperlipidemia, obesity, metabolic syndrome, diabetic nephropathy, diabetic retinopathy, diabetic vasculopathy, and diabetic neuropathy), and involve long-term management.

Growth factor receptor bound protein 14 (GRB14) is an adapter protein that interacts with receptor tyrosine kinases, including insulin receptor and IGF receptors. GRB14 negatively regulates signaling through insulin receptor and IGF-1 receptor and are associated with decreased insulin sensitivity. GRB14-knockout mice have been reported to have improved insulin signaling in the liver and skeletal muscle. GRB14 knockdown in the liver, white adipose tissues, and heart has been reported to improve glucose homeostasis in diet-induced obese mice. Accordingly, inhibition of GRB14 may offer therapeutic advantages for insulin resistance, pre-diabetes, and diabetes.

SUMMARY OF THE DISCLOSURE

The present disclosure provides iRNA compositions which effect the RNA-induced silencing complex (RISC)-mediated cleavage of RNA transcripts of a growth factor receptor bound protein 14 (GRB14) gene. The GRB14 gene may be within a cell, *e.g.*, a cell within a subject, such as a human. The present disclosure also provides methods of using the iRNA compositions of the disclosure for inhibiting the expression of a GRB14 gene and/or for treating a subject who would benefit from inhibiting or reducing the expression of a GRB14 gene, *e.g.*, a subject suffering or prone to suffering from a GRB14-associated disease, for example, diabetes.

Accordingly, in one aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4.

In another aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein said antisense strand comprises a region of complementarity to an mRNA encoding GRB14 which comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from any one of the antisense sequences listed in Tables 2-7 or 15-16. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein said antisense strand comprises a region of complementarity to an mRNA encoding GRB14 which comprises at least 15 contiguous nucleotides from any one of the antisense sequences listed in Tables 2-7 or 15-16.

In various embodiments of the dsRNA agents provided herein, the dsRNA agent targets a hotspot region of an mRNA encoding GRB14. In one aspect, the present disclosure provides a dsRNA agent that targets a hotspot region of a GRB14 mRNA.

In one embodiment, the dsRNA agent comprises at least one modified nucleotide. In one embodiment, substantially all of the nucleotides of the sense strand comprise a modification. In another embodiment, substantially all of the nucleotides of the antisense strand comprise a modification. In yet another embodiment,

substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand comprise a modification.

In one aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4, wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand are modified nucleotides, and wherein the sense strand is conjugated to a ligand attached at the 3'-terminus. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4, wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand are modified nucleotides, and wherein the sense strand is conjugated to a ligand attached at the 3'-terminus.

In one aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16, wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand are modified nucleotides, and wherein the sense strand is conjugated to a ligand attached at the 3'-terminus. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16, and the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16, wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand are modified nucleotides, and wherein the sense strand is conjugated to a ligand attached at the 3'-terminus.

In one embodiment, all of the nucleotides of the sense strand comprise a modification. In another embodiment, all of the nucleotides of the antisense strand comprise a modification. In yet another embodiment, all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a modification.

In one embodiment, the at least one modified nucleotide is selected from the group consisting of a deoxy-nucleotide, a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-O-allyl-modified nucleotide, 2'-C-alkyl-modified nucleotide, a 2'-methoxyethyl modified nucleotide, a 2'-O-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a phosphorothioate group, a nucleotide comprising a methylphosphonate group, a nucleotide comprising a 5'-phosphate, a nucleotide comprising a 5'-phosphate mimic, a glycol modified nucleotide, and a 2-O-(N-methylacetamide) modified nucleotide, and combinations thereof.

In one embodiment, the at least one modified nucleotide is a 2'-O-methyl and/or a 2'-fluoro modification.

The region of complementarity may be at least 17 nucleotides in length; 19 to 30 nucleotides in length; 19-25 nucleotides in length; or 21 to 23 nucleotides in length.

Each strand may be no more than 30 nucleotides in length, *e.g.,* each strand is independently 19-30 nucleotides in length; each strand is independently 19-25 nucleotides in length; each strand is independently 21-23 nucleotides in length.

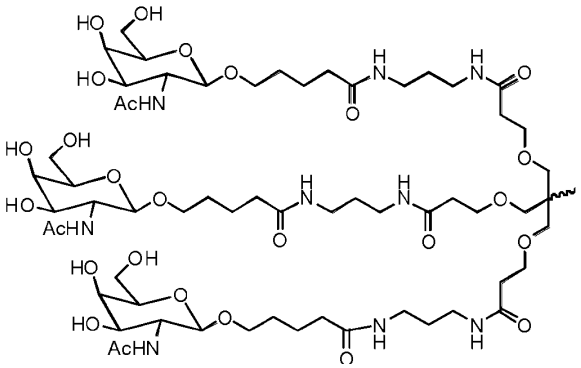
The dsRNA may include at least one strand that comprises a 3' overhang of at least 1 nucleotide; or at least one strand that comprises a 3' overhang of at least 2 nucleotides.

In some embodiment, the dsRNA agent further comprises a ligand.

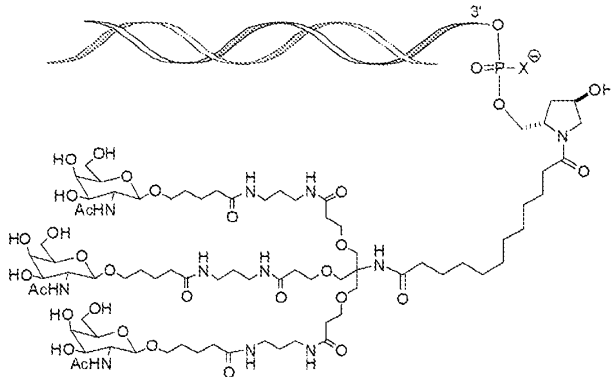
In one embodiment, the ligand is conjugated to the 3' end of the sense strand of the dsRNA agent.

In one embodiment, the ligand is an N-acetylgalactosamine (GalNAc) derivative.

In one embodiment, the ligand is



In one embodiment, the dsRNA agent is conjugated to the ligand as shown in the following schematic



and, wherein X is O or S.

In one embodiment, the X is O.

In one embodiment, the present disclosure provides a dsRNA agent wherein (a) the sense strand comprises the nucleotide sequence CAAAACUUUCGUACUGUCAAA (SEQ ID NO: 8770) and the antisense strand comprises the nucleotide sequence UUUGACAGUACGAAAGUUUUGGG (SEQ ID NO: 8784); (b) the sense strand comprises the nucleotide sequence AAGACUUGGAUUGACUUUACA (SEQ ID NO: 8771) and the antisense strand comprises the nucleotide sequence UGUAAAGUCAAUCCAAGUCUUUG (SEQ ID NO: 8785); (c) the sense strand comprises the nucleotide sequence UUGACUUUACAUUCAUCAUUA (SEQ ID NO: 8777) and the antisense strand comprises the nucleotide sequence UAAUGATGAAUGUAAAGUCAAUC (SEQ ID NO: 8791); (d) the sense strand comprises the nucleotide sequence UUAUGCCAAAUAUGAGUUCUA (SEQ ID NO: 8781) and the antisense strand comprises the nucleotide sequence UAGAACTCAUATUUGGCAUAAUU (SEQ ID NO: 8795); (e) the sense strand comprises the nucleotide sequence UGCAAGUUGAAACAUUAUUGA (SEQ ID NO: 8783) and the antisense strand comprises the nucleotide sequence

UCAATAAUGUUTCAACUUGCAAG (SEQ ID NO: 8797); or (f) the sense strand comprises the nucleotide sequence UAUCCUGAAAUUCAUGGUUUA (SEQ ID NO: 7595) and the antisense strand comprises the nucleotide sequence UAAACCAUGAATUUCAGGAUAUG (SEQ ID NO: 7863).

In one embodiment, the present disclosure provides a dsRNA agent wherein (a) the sense strand consists of the nucleotide sequence CAAAACUUUCGUACUGUCAAA (SEQ ID NO: 8770) and the antisense strand consists of the nucleotide sequence UUUGACAGUACGAAAGUUUUGGG (SEQ ID NO: 8784); (b) the sense strand consists of the nucleotide sequence AAGACUUGGAUUGACUUUACA (SEQ ID NO: 8771) and the antisense strand consists of the nucleotide sequence UGUAAAGUCAAUCCAAGUCUUUG (SEQ ID NO: 8785); (c) the sense strand consists of the nucleotide sequence UUGACUUUACAUUCAUCAUUA (SEQ ID NO: 8777) and the antisense strand consists of the nucleotide sequence UAAUGATGAAUGUAAAGUCAAUC (SEQ ID NO: 8791); (d) the sense strand consists of the nucleotide sequence UUAUGCCAAAUAUGAGUUCUA (SEQ ID NO: 8781) and the antisense strand consists of the nucleotide sequence UAGAACTCAUATUUGGCAUAAUU (SEQ ID NO: 8795); (e) the sense strand consists of the nucleotide sequence UGCAAGUUGAAACAUUAUUGA (SEQ ID NO: 8783) and the antisense strand consists of the nucleotide sequence UCAATAAUGUUTCAACUUGCAAG (SEQ ID NO: 8797); or (f) the sense strand consists of the nucleotide sequence UAUCCUGAAAUUCAUGGUUUA (SEQ ID NO: 7595) and the antisense strand consists of the nucleotide sequence UAAACCAUGAATUUCAGGAUAUG (SEQ ID NO: 7863).

In one embodiment, the present disclosure provides a dsRNA agent wherein (a) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8798 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8812; (b) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8799 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8813; (c) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8805 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8819; (d) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8809 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8823; (e) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8811 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8825; or (f) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8131 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8399.

In one embodiment, the region of complementarity comprises any one of the antisense sequences in Tables 2-7 or 15-16.

In one embodiment, the at least one modified nucleotide is selected from the group consisting of LNA, HNA, CeNA, 2′-methoxyethyl, 2′-O-alkyl, 2′-O-allyl, 2′-C- allyl, 2′-fluoro, 2'-O-methyl, 2′-deoxy, and combinations thereof.

In one embodiment, the at least one modified nucleotide is a 2′-O-methyl or a 2′-fluoro modification.

In one embodiment, at least one strand of the dsRNA agent may comprise a 3' overhang of at least 1 nucleotide; or a 3' overhang of at least 2 nucleotides.

In one embodiment, the dsRNA agent further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

In one embodiment, the phosphorothioate or methylphosphonate internucleotide linkage is at the 3'-terminus of one strand. In one embodiment, the strand is the antisense strand. In another embodiment, the strand is the sense strand.

In one embodiment, the phosphorothioate or methylphosphonate internucleotide linkage is at the 5'-terminus of one strand. In one embodiment, the strand is the antisense strand. In another embodiment, the strand is the sense strand.

In one embodiment, the strand is the antisense strand. In another embodiment, the strand is the sense strand.

In one embodiment, the phosphorothioate or methylphosphonate internucleotide linkage is at both the 5'- and 3'-terminus of one strand.

In one embodiment, the base pair at the 1 position of the 5′-end of the antisense strand of the duplex is an AU base pair.

In one embodiment, the sense strand has a total of 21 nucleotides and the antisense strand has a total of 23 nucleotides.

In one aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting the expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4, wherein substantially all of the nucleotides of the sense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus, wherein substantially all of the nucleotides of the antisense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification, a 2'-fluoro modification, and a deoxy-nucleotide, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two

phosphorothioate internucleotide linkages at the 3'-terminus, and wherein the sense strand is conjugated to one or more GalNAc derivatives attached through a monovalent, bivalent or trivalent branched linker at the 3'-terminus. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 1 and 3, and the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of SEQ ID NOs: 2 and 4, wherein substantially all of the nucleotides of the sense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus, wherein substantially all of the nucleotides of the antisense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and wherein the sense strand is conjugated to one or more GalNAc derivatives attached through a monovalent, bivalent or trivalent branched linker at the 3'-terminus.

In one aspect, the present disclosure provides a double stranded ribonucleic acid (dsRNA) agent for inhibiting the expression of growth factor receptor bound protein 14 (GRB14) in a cell. The dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16, and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16, wherein substantially all of the nucleotides of the sense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus, wherein substantially all of the nucleotides of the antisense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification, a 2'-fluoro modification, and a deoxy-nucleotide, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and wherein the sense strand is conjugated to one or more GalNAc derivatives attached through a monovalent, bivalent or trivalent branched linker at the 3'-terminus. In some embodiments, the dsRNA agent includes a sense strand and an antisense strand forming a double stranded region, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16, and the antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16, wherein substantially all of the nucleotides of the sense strand comprise a modification

selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus, wherein substantially all of the nucleotides of the antisense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification, wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and wherein the sense strand is conjugated to one or more GalNAc derivatives attached through a monovalent, bivalent or trivalent branched linker at the 3'-terminus.

In one embodiment, all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand are modified nucleotides.

In one embodiment, the region of complementarity comprises any one of the antisense sequences listed in Tables 2-7 or 15-16. In one embodiment, the agent is selected from the group consisting of AD-2217254, AD-2217251, AD-2217248, AD-2217250, AD-2217245, AD-2217252, AD-2217253, AD-2217246, AD-2217262, AD-2217258, AD-2217255, AD-2217257, or AD-2123142.

In one embodiment, the sense strand and the antisense strand comprise nucleotide sequences selected from the group consisting of the nucleotide sequences of any one of the agents listed in Tables 2-7 or 15-16.

The present disclosure also provides cells, vectors, and pharmaceutical compositions which include any of the dsRNA agents of the disclosure. The dsRNA agents may be formulated in an unbuffered solution, *e.g.*, saline or water, or in a buffered solution, *e.g.*, a solution comprising acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof. In one embodiment, the buffered solution is phosphate buffered saline (PBS).

In one aspect, the present disclosure provides a method of inhibiting growth factor receptor bound protein 14 (GRB14) expression in a cell. The method includes introducing into the cell a dsRNA agent or a pharmaceutical composition of the disclosure, thereby inhibiting expression of GRB14 in the cell.

The cell may be within a subject, such as a human subject.

In one embodiment, the GRB14 expression is inhibited by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or to below the level of detection of GRB14 expression.

In one embodiment, the human subject suffers from a GRB14-associated disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is diabetes. In one embodiment the diabetes is type 2 diabetes. In another embodiment, the diabetes is type 1 diabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is prediabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is insulin resistance. In one embodiment, the GRB14-associated disease, disorder, or condition is a diabetes-related disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is obesity, diabetic neuropathy, diabetic

nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

In one aspect, the present disclosure provides a method of inhibiting the expression of GRB14 in a subject. The methods include administering to the subject a therapeutically effective amount of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby inhibiting the expression of GRB14 in the subject. In one embodiment, the subject has a GRB14-associated disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is diabetes. In one embodiment the diabetes is type 2 diabetes. In another embodiment, the diabetes is type 1 diabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is prediabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is insulin resistance. In one embodiment, the GRB14-associated disease, disorder, or condition is a diabetes-related disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

In another aspect, the present disclosure provides a method of treating a subject suffering from a GRB14-associated disease, disorder, or condition. The method includes administering to the subject a therapeutically effective amount of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby treating the subject suffering from a GRB14-associated disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is diabetes. In one embodiment the diabetes is type 2 diabetes. In another embodiment, the diabetes is type 1 diabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is prediabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is insulin resistance. In one embodiment, the GRB14-associated disease, disorder, or condition is a diabetes-related disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

In another aspect, the present disclosure provides a method of preventing at least one symptom in a subject having a GRB14-associated disease, disorder, or condition. The method includes administering to the subject a prophylactically effective amount of the agent of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby preventing at least one symptom in a subject having a GRB14-associated disease, disorder, or condition. In one embodiment, the GRB14-associated disease, disorder, or condition is diabetes. In one embodiment the diabetes is type 2 diabetes. In another embodiment, the diabetes is type 1 diabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is prediabetes. In one embodiment, the GRB14-associated disease, disorder, or condition is insulin resistance. In one embodiment, the GRB14-associated disease, disorder, or condition is a diabetes-related disease, disorder, or condition. In one

embodiment, the GRB14-associated disease, disorder, or condition is obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

In another aspect, the present disclosure provides a method of reducing the risk of developing type 2 diabetes in a subject. The method includes administering to the subject a prophylactically effective amount or a prophylactically effective amount of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby reducing the risk of developing type 2 diabetes in the subject.

In another aspect, the present disclosure provides a method of increasing insulin sensitivity in a subject. The method includes administering to the subject a therapeutically effective amount of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby increasing insulin sensitivity in the subject. In one embodiment, the insulin sensitivity is hepatic insulin sensitivity.

In another aspect, the present disclosure provides a method of reversing type 2 diabetes in a subject. The method includes administering to the subject a therapeutically effective amount of a dsRNA agent or a pharmaceutical composition of the disclosure, thereby reversing type 2 diabetes in the subject.

In one embodiment, the subject is obese.

In one embodiment, the methods and uses of the disclosure further include administering an additional therapeutic to the subject.

In one embodiment, the dsRNA agent is administered to the subject at a dose of about 0.01 mg/kg to about 10 mg/kg or about 0.5 mg/kg to about 50 mg/kg.

The agent may be administered to the subject intravenously, intramuscularly, or subcutaneously. In one embodiment, the agent is administered to the subject subcutaneously.

In one embodiment, the methods and uses of the disclosure further include determining, the level of GRB14 in the subject.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 depicts the results of *in vivo* screening in PBX-mice. The graph shows the percent of GRB14 mRNA (left bar) and protein (right bar) in liver relative to the PBS mean for AD-2217245 (5 mpk), AD-2217246 (5 mpk), AD-2217252 (5 mpk), AD-2217262 (5 mpk), and AD-213142 (10 mpk x3).

FIG. 2 depicts the results of *in vivo* screening in non-human primates (NHP). The graph shows the effect of administration of a single 20 mg/kg dose and 3 mg/kg dose of the selected duplexes on the level of GRB14 mRNA in liver at Day 22 post-dose.

FIG. 3 depicts the results of *in vivo* screening in non-human primates (NHP). The graph shows the effect of administration of a single 20 mg/kg dose and 3 mg/kg dose of the selected duplexes on the level of GRB14 protein in liver at Day 22 and Day 57 post-dose.

FIG. 4A and FIG. 4B show the results of an *in vivo* study in genetically obese mice (Ob/Ob). FIG. 4A shows the GRB14 expression after treatment and FIG. 4B illustrates the %HbA1c in the mice after treatment.

FIG. 5A and FIG. 5B show the results of an *in vivo* study in high fat diet (HFD) treated mice. FIG. 5A depicts the results of a Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) taken at week 8. FIG. 5B depicts the GRB14 expression.

FIG. 6A, FIG. 6B, and FIG. 6C show the results of an *in vivo* study in diet induced obese (DIO) mice. FIG. 6A shows the results of a glucose tolerance test in DIO mice administered 10 mg/kg of the selected duplexes compared to DIO and lean mouse controls. FIG. 6B shows the results of an insulin tolerance test in DIO mice administered 10 mg/kg of the selected duplexes compared to DIO and lean mouse controls. FIG. 6C shows the body weight at week 8 of DIO mice administered 10 mg/kg of the selected duplexes compared to DIO and lean mouse controls.

DETAILED DESCRIPTION OF THE DISCLOSURE

The present disclosure provides iRNA compositions, which effect the RNA-induced silencing complex (RISC)-mediated cleavage of RNA transcripts of a GRB14 gene. The GRB14 gene may be within a cell, *e.g.,* a cell within a subject, such as a human. The present disclosure also provides methods of using the iRNA compositions of the disclosure for inhibiting the expression of a GRB14 gene, and for treating a subject who would benefit from inhibiting or reducing the expression of a GRB14 gene, *e.g.,* a subject suffering or prone to suffering from a GRB14-associated disease disorder, or condition, such as a subject suffering or prone to suffering from type 2 diabetes, type 1 diabetes, prediabetes, insulin resistance, or a diabetes-related disease, disorder, or condition, such as obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc.

The iRNAs of the disclosure targeting GRB14 may include an RNA strand (the antisense strand) having a region which is about 30 nucleotides or less in length, *e.g.*, 15-30, 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 nucleotides in length, which region is substantially complementary to at least part of an mRNA transcript of a GRB14 gene.

In some embodiments, one or both of the strands of the double stranded RNAi agents of the disclosure is up to 66 nucleotides in length, *e.g.*, 36-66, 26-36, 25-36, 31-60, 22-43, 27-53 nucleotides in length, with a region of at least 19 contiguous nucleotides that is substantially complementary to at least a part of an mRNA

transcript of a GRB14 gene. In some embodiments, such iRNA agents having longer length antisense strands may include a second RNA strand (the sense strand) of 20-60 nucleotides in length wherein the sense and antisense strands form a duplex of 18-30 contiguous nucleotides.

The use of the iRNA agents described herein enables the targeted degradation of mRNAs of a GRB14 gene in mammals.

Very low dosages of the iRNAs, in particular, can specifically and efficiently mediate RNA interference (RNAi), resulting in significant inhibition of expression of a GRB14 gene. Thus, methods and compositions including these iRNAs are useful for treating a subject who would benefit from inhibiting or reducing the expression of a GRB14 gene, *e.g.,* a subject that would benefit from a reduction of inflammation of the liver, *e.g.,* a subject suffering or prone to suffering from a GRB14-associated disease disorder, or condition such as diabetes type 2, diabetes type 1, insulin resistance, or a diabetes-related disease, disorder, or condition, such as obesity, diabetic nephropathy, diabetic neurodpathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc.

The following detailed description discloses how to make and use compositions containing iRNAs to inhibit the expression of a GRB14 gene, as well as compositions and methods for treating subjects having diseases and disorders that would benefit from inhibition and/or reduction of the expression of this gene.

I. Definitions

In order that the present disclosure may be more readily understood, certain terms are first defined. In addition, it should be noted that whenever a value or range of values of a parameter are recited, it is intended that values and ranges intermediate to the recited values are also intended to be part of this disclosure.

The articles “a” and “an” are used herein to refer to one or to more than one (*i.e.*, to at least one) of the grammatical object of the article. By way of example, “an element” means one element or more than one element, *e.g.*, a plurality of elements.

The term "including" is used herein to mean, and is used interchangeably with, the phrase "including but not limited to".

The term "or" is used herein to mean, and is used interchangeably with, the term "and/or," unless context clearly indicates otherwise.

The term “about” is used herein to mean within the typical ranges of tolerances in the art. For example, “about” can be understood as about 2 standard deviations from the mean. In certain embodiments, about means $\pm$10%. In certain embodiments, about means $\pm$5%. When about is present before a series of numbers or a range, it is understood that “about” can modify each of the numbers in the series or range.

The term “GRB14,” also known as “growth factor receptor bound protein 14,” refers to the well-known gene encoding a growth factor receptor bound protein 14 protein from any vertebrate or mammalian

source, including, but not limited to, human, bovine, chicken, rodent, mouse, rat, porcine, ovine, primate, monkey, and guinea pig, unless specified otherwise.

The term also refers to fragments and variants of native GRB14 that maintain at least one *in vivo* or *in vitro* activity of a native GRB14. The term encompasses full-length unprocessed precursor forms of GRB14 as well as mature forms resulting from post-translational cleavage of the signal peptide and forms resulting from proteolytic processing.

The human GRB14 gene has 18 exons. Two variants of the human GRB14 gene have been identified, transcript variants 1 and 2. The nucleotide and amino acid sequence of a human GRB14 trascript variant 1 can be found in, for example, GenBank Reference Sequence: NM_004490.3 (SEQ ID NO: 1; reverse complement, SEQ ID NO: 2); and the nucleotide and amino acid sequence of a human GRB14 transcript variant 2 can be found in, for example, GenBank Reference Sequence: NM_001303422.2 (SEQ ID NO: 3; reverse complement, SEQ ID NO: 4).

The human GRB14 gene is located in the chromosomal region 2q24.3. The nucleotide sequence of the genomic region of human chromosome harboring the GRB14 gene may be found in, for example, the Genome Reference Consortium Human Build 38 (also referred to as Human Genome build 38 or GRCh38) available at GenBank. The nucleotide sequence of the genomic region of human chromosome 2 harboring the GRB14 gene may also be found at, for example, GenBank Accession No. NC_000002.12, corresponding to nucleotides 164,492,417-164,622,959 of human chromosome 2. The nucleotide sequence of the human GRB14 gene may be found in, for example, GenBank Accession No. NG_052839.1, corresponding to nucleotides 5,369-134,434.

The nucleotide and amino acid sequence of a mouse (*Mus musculus*) GRB14 transcript can be found in, for example, GenBank Reference Sequence: NM_016719.1 (SEQ ID NO: 5; reverse complement, SEQ ID NO: 6). The nucleotide and amino acid sequence of a rat (*Rattus norvegicus*) GRB14 transcript can be found in, for example, GenBank Reference Sequence: NM_031623.1 (SEQ ID NO: 7; reverse complement, SEQ ID NO: 8). There are three predicted transcript variants of the Rhesus monkey (Macaca mulatta) GRB14 gene. The nucleotide and amino acid sequence of a Rhesus monkey GRB14 transcript variant 1 can be found in, for example, GenBank Reference Sequence: XM_015110244.2 (SEQ ID NO: 9; reverse complement, SEQ ID NO: 10); the nucleotide and amino acid sequence of a Rhesus monkey GRB14 transcript variant 2 can be found in, for example, GenBank Reference Sequence: XM_028830779.1 (SEQ ID NO: 11; reverse complement, SEQ ID NO: 12); and the nucleotide and amino acid sequence of a Rhesus monkey GRB14 transcript variant 3 can be found in, for example, GenBank Reference Sequence: XM_015110245.2 (SEQ ID NO: 13; reverse complement, SEQ ID NO: 14). There are three predicted transcript variants of the rabbit (*Oryctolagus cuniculus*) GRB14 gene. The nucleotide and amino acid sequence of a rabbit GRB14 transcript variant 1 can be found in, for example, GenBank Reference Sequence: XM_008258679.2 (SEQ ID NO: 15;

reverse complement, SEQ ID NO: 16); the nucleotide and amino acid sequence of a rabbit GRB14 transcript variant 2 can be found in, for example, GenBank Reference Sequence: XM_017342897.1 (SEQ ID NO: 17; reverse complement, SEQ ID NO: 18); and the nucleotide and amino acid sequence of a rabbit GRB14 transcript variant 3 can be found in, for example, GenBank Reference Sequence: XM_017342898.1 (SEQ ID NO: 19; reverse complement, SEQ ID NO: 20).

Additional examples of GRB14 mRNA sequences are readily available using publicly available databases, *e.g.*, GenBank, UniProt, and OMIM. Additional information on GRB14 can be found, for example, at www.ncbi.nlm.nih.gov/gene/2888. The term GRB14 as used herein also refers to variations of the GRB14 gene including variants provided in the clinical variant database, for example, at www.ncbi.nlm.nih.gov/clinvar/?term=GRB14[gene].

The term "GRB14" as used herein also refers to a particular polypeptide expressed in a cell by naturally occurring DNA sequence variations of the GRB14 gene, such as a single nucleotide polymorphism in the GRB14 gene. Numerous SNPs within the GRB14 gene have been identified and may be found at, for example, NCBI dbSNP (see, *e.g.*, www.ncbi.nlm.nih.gov/snp).

Growth factor receptor-bound protein 14 (GRB14) is a protein belonging to a small family of adapter proteins that further comprises growth factor receptor-bound protein 7 (GRB7) and growth factor receptor-bound protein 10 (GRB10). These adapter proteins interact with a number of receptor tyrosine kinases and signaling molecules. GRB14 binds an insulin receptor (IR), epidermal growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor (FGFR), as well as Tek/Tie2 (Han et al. (2001) *Oncogene* 20:6351-6321). No binding of GRB14 to insulin-like growth factor receptor (IGFR) has been reported, but IGFR was sensitive to inhibition of tyrosine kinase activity by GRB14 *in vitro*, though less so than IR (Holt et al. (2005) *Biochem. J.* 388:393–406).

GRB14 is a major negative regulator of insulin and IGF-1 metabolic pathways, whereas GRB7 regulates focal adhesion kinase (FAK)-mediated cell migration. GRB7/10/14 are most abundantly expressed in the pancreas, with GRB14 having relatively broad expression profiles (Han et al. (2001) *Oncogene* 20:6351-6321). GRB14 mRNA and protein are expressed strongly in skeletal muscle and white adipose tissue, two major insulin target tissues, as well as heart and kidney (Holt et al. (2005) *Biochem. J.* 388:393–406). Strong GRB14 expression is found also in the pancreatic islets, liver and in retinal rod photoreceptor cells (Desbuquois et al. (2013) *FEBS J* 280(3):794-816; Holt et al. (2005) *Biochem. J.* 388:393–406).

Insulin is a major hormonal regulator of glucose and lipid homeostasis, particularly in the target tissues of muscle, fat, and liver. Overexpression of GRB14 blocks the interaction of PTP-1B with the insulin receptor, shielding it from dephosphorylation and at the same time inhibits Akt/PKB and ERK1/2 activation. Furthermore, in Grb14-deficient mice, insulin receptor tyrosine phosphorylation in the liver is decreased, and insulin activation of IRS and Akt/PKB is augmented (Dufresne et al. (2005) *Endocrinology* 146(10):4399–

4409). Overexpression of GRB14 in Chinese hamster ovary cells inhibited insulin-stimulated DNA and glycogen synthesis. GRB14 inhibited IR substrate phosphorylation in vitro (Deng et al. (2003) *J Biol Chem* 278(41):39311-22). Targeted deletion of the GRB14 gene has been shown to improve insulin sensitivity and glucose homeostasis, suggesting GRB14 negatively regulates insulin signaling and action (Wang et al. (2007) *Mol Cell Biol* (18):6497-505). Disruption of the GRB14 gene in mice results in a slight decrease in body mass and liver mass, an increase in heart mass, and an improved in vivo glucose tolerance and insulin sensitivity. It also enhances insulin-induced stimulation of glucose transport in skeletal muscle, as well as glycogen synthesis in liver and muscle (Desbuquois et al. (2013) *FEBS J* 280(3):794-816). GRB14 mRNA and protein expression were found to be increased by 75–100% in adipose tissue, but not in liver, in two rodent models of type 2 diabetes, and mRNA expression was increased by 43% in subcutaneous adipose tissue, but was not significantly altered in skeletal muscle, of human type 2 diabetics (Holt et al. (2005) *Biochem. J.* 388:393–406).

Removal of GRB14 decreases receptor phosphorylation of insulin receptor (IR) and IGF-I receptor, presumably due to increased phosphatase access, and is coupled with enhanced downstream signaling. As described above, GRB14 protein is expressed prominently in insulin target tissues, including the liver, skeletal muscle, and adipose tissue. Variants of GRB14 have been associated with obesity and/or insulin resistance. A number of other studies have examined the association of GRB14 single nucleotide polymorphisms with type 2 diabetes and/or associated metabolic profiles, each of which is hereby incorporated by reference in its entirety (Di Paula, et al., (2010) *J. Intern. Med.* 267(1):132–133; Di Paula, et al., (2006) *Diabetes Care* 29(5):1181-1182; Manning et al. (2013) *Nat. Genet.* 44(6):659–669; Rampersaud et al. (2007) *Diabetes* 56:3053-3062; Scott et al. (2012) *Nat. Genet.* 44(9):991–1005; Kooner et al. (2013) *Nat Genet.* 43(10):984–989). In animal studies, the germline Grb14-knockout mice have improved insulin signaling in liver and skeletal muscle (Cooney et al. (2004) *Embo J.* 23:582-593). Grb14 knockdown in the liver, white adipose tissues, and heart improved glucose homeostasis in diet-induced obese mice (Ding et al. (2020) *Sci Rep.* 10:3417).

Each protein of the GRB7/10/14 family comprises an N-terminal proline-rich region, a Ras-associating (RA) domain, a pleckstrin homology (PH) domain, a C-terminal Src homology 2 (SH2) domain, and a conserved region referred to as the BPS domain (named for being between the PH and SH2 domains) or the phosphorylated insulin receptor-interacting region (PIR) that is unique to the family. GRB7/10/14 family members share high sequence identity (approximately 60-70%) in the SH2 domain and a smaller sequence identify with members of the SH2B family of adapter proteins (approximately 25-30%).

As used herein, "target sequence" refers to a contiguous portion of the nucleotide sequence of an mRNA molecule formed during the transcription of a GRB14 gene, including mRNA that is a product of RNA processing of a primary transcription product. In one embodiment, the target portion of the sequence will be at

least long enough to serve as a substrate for iRNA-directed cleavage at or near that portion of the nucleotide sequence of an mRNA molecule formed during the transcription of a GRB14 gene.

The target sequence of a GRB14 gene may be from about 9-36 nucleotides in length, *e.g.*, about 15-30 nucleotides in length. For example, the target sequence can be from about 15-30 nucleotides, 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 nucleotides in length. Ranges and lengths intermediate to the above recited ranges and lengths are also contemplated to be part of the disclosure.

As used herein, the term "strand comprising a sequence" refers to an oligonucleotide comprising a chain of nucleotides that is described by the sequence referred to using the standard nucleotide nomenclature.

"G," "C," "A," "T" and "U" each generally stand for a nucleotide that contains guanine, cytosine, adenine, thymidine and uracil as a base, respectively. However, it will be understood that the term "ribonucleotide" or "nucleotide" can also refer to a modified nucleotide, as further detailed below, or a surrogate replacement moiety (see, *e.g.,* Table 1). The skilled person is well aware that guanine, cytosine, adenine, and uracil can be replaced by other moieties without substantially altering the base pairing properties of an oligonucleotide comprising a nucleotide bearing such replacement moiety. For example, without limitation, a nucleotide comprising inosine as its base can base pair with nucleotides containing adenine, cytosine, or uracil. Hence, nucleotides containing uracil, guanine, or adenine can be replaced in the nucleotide sequences of dsRNA featured in the disclosure by a nucleotide containing, for example, inosine. In another example, adenine and cytosine anywhere in the oligonucleotide can be replaced with guanine and uracil, respectively to form G-U Wobble base pairing with the target mRNA. Sequences containing such replacement moieties are suitable for the compositions and methods featured in the disclosure.

The terms "iRNA", "RNAi agent," "iRNA agent,", "RNA interference agent" as used interchangeably herein, refer to an agent that contains RNA as that term is defined herein, and which mediates the targeted cleavage of an RNA transcript *via* an RNA-induced silencing complex (RISC) pathway. iRNA directs the sequence-specific degradation of mRNA through a process known as RNA interference (RNAi). The iRNA modulates, *e.g.,* inhibits, the expression of the GRB14 gene in a cell, *e.g.,* a cell within a subject, such as a mammalian subject.

In one embodiment, an RNAi agent of the disclosure includes a single stranded RNA that interacts with a target RNA sequence, *e.g.,* a GRB14 target mRNA sequence, to direct the cleavage of the target RNA. Without wishing to be bound by theory it is believed that long double stranded RNA introduced into cells is broken down into siRNA by a Type III endonuclease known as Dicer (Sharp *et al.* (2001) *Genes Dev.* 15:485). Dicer, a ribonuclease-III-like enzyme, processes the dsRNA into 19-23 base pair short interfering RNAs with

characteristic two base 3' overhangs (Bernstein, *et al.*, (2001) *Nature* 409:363). The siRNAs are then incorporated into an RNA-induced silencing complex (RISC) where one or more helicases unwind the siRNA duplex, enabling the complementary antisense strand to guide target recognition (Nykanen, *et al.*, (2001) *Cell* 107:309). Upon binding to the appropriate target mRNA, one or more endonucleases within the RISC cleave the target to induce silencing (Elbashir, *et al.*, (2001) *Genes Dev.* 15:188). Thus, in one aspect the disclosure relates to a single stranded RNA (sssiRNA) generated within a cell and which promotes the formation of a RISC complex to effect silencing of the target gene, *i.e.*, a GRB14 gene. Accordingly, the term "siRNA" is also used herein to refer to an RNAi as described above.

In another embodiment, the RNAi agent may be a single-stranded RNAi agent that is introduced into a cell or organism to inhibit a target mRNA. Single-stranded RNAi agents (ssRNAi) bind to the RISC endonuclease, Argonaute 2, which then cleaves the target mRNA. The single-stranded siRNAs are generally 15-30 nucleotides and are chemically modified. The design and testing of single-stranded RNAi agents are described in U.S. Patent No. 8,101,348 and in Lima *et al.*, (2012) *Cell* 150: 883-894, the entire contents of each of which are hereby incorporated herein by reference. Any of the antisense nucleotide sequences described herein may be used as a single-stranded siRNA as described herein or as chemically modified by the methods described in Lima *et al.*, (2012) *Cell* 150:883-894.

In another embodiment, an "iRNA" for use in the compositions and methods of the disclosure is a double-stranded RNA and is referred to herein as a "double stranded RNAi agent," "double-stranded RNA (dsRNA) molecule," "dsRNA agent," or "dsRNA". The term "dsRNA", refers to a complex of ribonucleic acid molecules, having a duplex structure comprising two anti-parallel and substantially complementary nucleic acid strands, referred to as having "sense" and "antisense" orientations with respect to a target RNA, *i.e.*, a GRB14 gene. In some embodiments of the disclosure, a double-stranded RNA (dsRNA) triggers the degradation of a target RNA, *e.g.*, an mRNA, through a post-transcriptional gene-silencing mechanism referred to herein as RNA interference or RNAi.

In general, the majority of nucleotides of each strand of a dsRNA molecule are ribonucleotides, but as described in detail herein, each or both strands can also include one or more non-ribonucleotides, *e.g.*, a deoxyribonucleotide and/or a modified nucleotide. In addition, as used in this specification, an "RNAi agent" may include ribonucleotides with chemical modifications; an RNAi agent may include substantial modifications at multiple nucleotides. As used herein, the term "modified nucleotide" refers to a nucleotide having, independently, a modified sugar moiety, a modified internucleotide linkage, and/or a modified nucleobase. Thus, the term modified nucleotide encompasses substitutions, additions or removal of, *e.g.*, a functional group or atom, to internucleoside linkages, sugar moieties, or nucleobases. The modifications suitable for use in the agents of the disclosure include all types of modifications disclosed herein or known in

the art. Any such modifications, as used in a siRNA type molecule, are encompassed by "RNAi agent" for the purposes of this specification and claims.

The duplex region may be of any length that permits specific degradation of a desired target RNA through a RISC pathway, and may range from about 9 to 36 base pairs in length, *e.g.*, about 15-30 base pairs in length, for example, about 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, or 36 base pairs in length, such as about 15-30, 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 base pairs in length. Ranges and lengths intermediate to the above recited ranges and lengths are also contemplated to be part of the disclosure.

The two strands forming the duplex structure may be different portions of one larger RNA molecule, or they may be separate RNA molecules. Where the two strands are part of one larger molecule, and therefore are connected by an uninterrupted chain of nucleotides between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure, the connecting RNA chain is referred to as a "hairpin loop." A hairpin loop can comprise at least one unpaired nucleotide. In some embodiments, the hairpin loop can comprise at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 23 or more unpaired nucleotides.

Where the two substantially complementary strands of a dsRNA are comprised by separate RNA molecules, those molecules need not, but can be covalently connected. Where the two strands are connected covalently by means other than an uninterrupted chain of nucleotides between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure, the connecting structure is referred to as a "linker." The RNA strands may have the same or a different number of nucleotides. The maximum number of base pairs is the number of nucleotides in the shortest strand of the dsRNA minus any overhangs that are present in the duplex. In addition to the duplex structure, an RNAi may comprise one or more nucleotide overhangs.

In one embodiment, an RNAi agent of the disclosure is a dsRNA, each strand of which comprises less than 30 nucleotides, *e.g.*, 17-27, 19-27, 17-25, 19-25, or 19-23, that interacts with a target RNA sequence, *e.g.*, a GRB14 target mRNA sequence, to direct the cleavage of the target RNA. In another embodiment, an RNAi agent of the disclosure is a dsRNA, each strand of which comprises 19-23 nucleotides, that interacts with a target RNA sequence, *e.g.*, a GRB14 target mRNA sequence, to direct the cleavage of the target RNA. In one embodiment, the sense strand is 21 nucleotides in length. In another embodiment, the antisense strand is 23 nucleotides in length.

As used herein, the term "nucleotide overhang" refers to at least one unpaired nucleotide that protrudes from the duplex structure of an iRNA, *e.g.*, a dsRNA. For example, when a 3'-end of one strand of a dsRNA extends beyond the 5'-end of the other strand, or vice versa, there is a nucleotide overhang. A dsRNA can comprise an overhang of at least one nucleotide; alternatively, the overhang can comprise at least two nucleotides, at least three nucleotides, at least four nucleotides, at least five nucleotides or more. A nucleotide overhang can comprise or consist of a nucleotide/nucleoside analog, including a deoxynucleotide/nucleoside. The overhang(s) can be on the sense strand, the antisense strand or any combination thereof. Furthermore, the nucleotide(s) of an overhang can be present on the 5'-end, 3'-end or both ends of either an antisense or sense strand of a dsRNA.

In one embodiment, the antisense strand of a dsRNA has a 1-10 nucleotide, *e.g.*, a 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotide, overhang at the 3'-end and/or the 5'-end. In one embodiment, the sense strand of a dsRNA has a 1-10 nucleotide, *e.g.*, a 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotide, overhang at the 3'-end and/or the 5'-end. In another embodiment, one or more of the nucleotides in the overhang is replaced with a nucleoside thiophosphate.

In certain embodiments, the overhang on the sense strand or the antisense strand, or both, can include extended lengths longer than 10 nucleotides, *e.g.*, 10-30 nucleotides, 10-25 nucleotides, 10-20 nucleotides or 10-15 nucleotides in length. In certain embodiments, an extended overhang is on the sense strand of the duplex. In certain embodiments, an extended overhang is present on the 3'end of the sense strand of the duplex. In certain embodiments, an extended overhang is present on the 5'end of the sense strand of the duplex. In certain embodiments, an extended overhang is on the antisense strand of the duplex. In certain embodiments, an extended overhang is present on the 3'end of the antisense strand of the duplex. In certain embodiments, an extended overhang is present on the 5'end of the antisense strand of the duplex. In certain embodiments, one or more of the nucleotides in the extended overhang is replaced with a nucleoside thiophosphate.

The terms "blunt" or "blunt ended" as used herein in reference to a dsRNA mean that there are no unpaired nucleotides or nucleotide analogs at a given terminal end of a dsRNA, *i.e.*, no nucleotide overhang. One or both ends of a dsRNA can be blunt. Where both ends of a dsRNA are blunt, the dsRNA is said to be blunt ended. To be clear, a "blunt ended" dsRNA is a dsRNA that is blunt at both ends, *i.e.*, no nucleotide overhang at either end of the molecule. Most often such a molecule will be double-stranded over its entire length.

The term "antisense strand" or "guide strand" refers to the strand of an iRNA, *e.g.*, a dsRNA, which includes a region that is substantially complementary to a target sequence, *e.g.*, a GRB14 mRNA.

As used herein, the term "region of complementarity" refers to the region on the antisense strand that is substantially complementary to a sequence, for example a target sequence, *e.g.*, a GRB14 nucleotide

sequence, as defined herein. Where the region of complementarity is not fully complementary to the target sequence, the mismatches can be in the internal or terminal regions of the molecule. Generally, the most tolerated mismatches are in the terminal regions, *e.g.*, within 5, 4, 3, or 2 nucleotides of the 5'- and/or 3'-terminus of the iRNA.

The term "sense strand" or "passenger strand" as used herein, refers to the strand of an iRNA that includes a region that is substantially complementary to a region of the antisense strand as that term is defined herein.

As used herein, the term "cleavage region" refers to a region that is located immediately adjacent to the cleavage site. The cleavage site is the site on the target at which cleavage occurs. In some embodiments, the cleavage region comprises three bases on either end of, and immediately adjacent to, the cleavage site. In some embodiments, the cleavage region comprises two bases on either end of, and immediately adjacent to, the cleavage site. In some embodiments, the cleavage site specifically occurs at the site bound by nucleotides 10 and 11 of the antisense strand, and the cleavage region comprises nucleotides 11, 12 and 13.

As used herein, and unless otherwise indicated, the term "complementary," when used to describe a first nucleotide sequence in relation to a second nucleotide sequence, refers to the ability of an oligonucleotide or polynucleotide comprising the first nucleotide sequence to hybridize and form a duplex structure under certain conditions with an oligonucleotide or polynucleotide comprising the second nucleotide sequence, as will be understood by the skilled person. Such conditions can, for example, be stringent conditions, where stringent conditions can include: 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA, 50°C or 70°C for 12-16 hours followed by washing (see, *e.g.*, "Molecular Cloning: A Laboratory Manual, Sambrook et al. (1989) Cold Spring Harbor Laboratory Press). Other conditions, such as physiologically relevant conditions as can be encountered inside an organism, can apply. The skilled person will be able to determine the set of conditions most appropriate for a test of complementarity of two sequences in accordance with the ultimate application of the hybridized nucleotides.

Complementary sequences within an iRNA, *e.g.*, within a dsRNA as described herein, include base-pairing of the oligonucleotide or polynucleotide comprising a first nucleotide sequence to an oligonucleotide or polynucleotide comprising a second nucleotide sequence over the entire length of one or both nucleotide sequences. Such sequences can be referred to as "fully complementary" with respect to each other herein. However, where a first sequence is referred to as "substantially complementary" with respect to a second sequence herein, the two sequences can be fully complementary, or they can form one or more, but generally not more than 5, 4, 3 or 2 mismatched base pairs upon hybridization for a duplex up to 30 base pairs, while retaining the ability to hybridize under the conditions most relevant to their ultimate application, *e.g.*, inhibition of gene expression via a RISC pathway. However, where two oligonucleotides are designed to form, upon hybridization, one or more single stranded overhangs, such overhangs shall not be regarded as

mismatches with regard to the determination of complementarity. For example, a dsRNA comprising one oligonucleotide 21 nucleotides in length and another oligonucleotide 23 nucleotides in length, wherein the longer oligonucleotide comprises a sequence of 21 nucleotides that is fully complementary to the shorter oligonucleotide, can yet be referred to as "fully complementary" for the purposes described herein.

"Complementary" sequences, as used herein, can also include, or be formed entirely from, non-Watson-Crick base pairs and/or base pairs formed from non-natural and modified nucleotides, in so far as the above requirements with respect to their ability to hybridize are fulfilled. Such non-Watson-Crick base pairs include, but are not limited to, G:U Wobble or Hoogstein base pairing.

The terms "complementary," "fully complementary" and "substantially complementary" herein can be used with respect to the base matching between the sense strand and the antisense strand of a dsRNA, or between the antisense strand of an iRNA agent and a target sequence, as will be understood from the context of their use.

As used herein, a polynucleotide that is "substantially complementary to at least part of" a messenger RNA (mRNA) refers to a polynucleotide that is substantially complementary to a contiguous portion of the mRNA of interest (*e.g.*, an mRNA encoding GRB14). For example, a polynucleotide is complementary to at least a part of a GRB14 mRNA if the sequence is substantially complementary to a non-interrupted portion of an mRNA encoding GRB14.

In some embodiments, the antisense strand polynucleotides disclosed herein are fully complementary to the target GRB14 sequence. In other embodiments, the antisense strand polynucleotides disclosed herein are substantially complementary to the target GRB14 sequence and comprise a contiguous nucleotide sequence which is at least about 80% complementary over its entire length to the equivalent region of the nucleotide sequence of SEQ ID NO: 1 or 3, or a fragment of SEQ ID NO: 1 or 3, such as about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about % 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, or about 99% complementary.

In one embodiment, an RNAi agent of the disclosure includes a sense strand that is substantially complementary to an antisense polynucleotide which, in turn, is complementary to a target GRB14 sequence, and wherein the sense strand polynucleotide comprises a contiguous nucleotide sequence which is at least about 80% complementary over its entire length to the equivalent region of the nucleotide sequence of SEQ ID NO: 2 or 4, or a fragment of any one of SEQ ID NO: 2 or 4, such as about 85%, about 86%, about 87%, about 88%, about 89%, about 90%, about % 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98%, or about 99% complementary.

In some embodiments, an iRNA of the disclosure includes an antisense strand that is substantially complementary to the target GRB14 sequence and comprises a contiguous nucleotide sequence which is at least about 80% complementary over its entire length to the equivalent region of the nucleotide sequence of

any one of the sense strands in Tables 2-7 or 15-16, or a fragment of any one of the sense strands in Tables 2-7 or 15-16, such as about 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% complementary, or 100% complementary.

The term "inhibiting," as used herein, is used interchangeably with "reducing," "silencing," "downregulating," "suppressing" and other similar terms, and includes any level of inhibition.

The phrase "inhibiting expression of a GRB14 gene," as used herein, includes inhibition of expression of any GRB14 gene (such as, *e.g.*, a mouse GRB14 gene, a rat GRB14 gene, a monkey GRB14 gene, or a human GRB14 gene) as well as variants or mutants of a GRB14 gene that encode a GRB14 protein, respectively.

"Inhibiting expression of a GRB14 gene" includes any level of inhibition of a GRB14 gene, *e.g.*, at least partial suppression of the expression of a GRB14 gene, such as an inhibition by at least about 20%. In certain embodiments, inhibition is by at least about 25%, at least about 30%, at least about 35%,at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, or at least about 99%.

The expression of a GRB14 gene may be assessed based on the level of any variable associated with GRB14 gene expression, *e.g.*, GRB14 mRNA level or GRB14 protein level. The expression of a GRB14 gene may also be assessed indirectly based on, for example, the enzymatic activity of GRB14 in a tissue sample, such as a liver sample. Inhibition may be assessed by a decrease in an absolute or relative level of one or more of these variables compared with a control level. The control level may be any type of control level that is utilized in the art, *e.g.*, a pre-dose baseline level, or a level determined from a similar subject, cell, or sample that is untreated or treated with a control (such as, *e.g.*, buffer only control or inactive agent control).

In one embodiment, at least partial suppression of the expression of a GRB14 gene, is assessed by a reduction of the amount of GRB14 mRNA which can be isolated from, or detected, in a first cell or group of cells in which a GRB14 gene is transcribed and which has or have been treated such that the expression of a GRB14 gene is inhibited, as compared to a second cell or group of cells substantially identical to the first cell or group of cells but which has or have not been so treated (control cells).

The degree of inhibition may be expressed in terms of:

$$\frac{(\text{mRNA in control cells}) - (\text{mRNA in treated cells})}{(\text{mRNA in control cells})} \bullet 100\%$$

The phrase "contacting a cell with an RNAi agent," such as a dsRNA, as used herein, includes contacting a cell by any possible means. Contacting a cell with an RNAi agent includes contacting a cell *in vitro* with the iRNA or contacting a cell *in vivo* with the iRNA. The contacting may be done directly or

indirectly. Thus, for example, the RNAi agent may be put into physical contact with the cell by the individual performing the method, or alternatively, the RNAi agent may be put into a situation that will permit or cause it to subsequently come into contact with the cell.

Contacting a cell *in vitro* may be done, for example, by incubating the cell with the RNAi agent. Contacting a cell *in vivo* may be done, for example, by injecting the RNAi agent into or near the tissue where the cell is located, or by injecting the RNAi agent into another area, *e.g.*, the bloodstream or the subcutaneous space, such that the agent will subsequently reach the tissue where the cell to be contacted is located. For example, the RNAi agent may contain and/or be coupled to a ligand, *e.g.*, GalNAc3, that directs the RNAi agent to a site of interest, *e.g.*, the liver. Combinations of *in vitro* and *in vivo* methods of contacting are also possible. For example, a cell may also be contacted *in vitro* with an RNAi agent and subsequently transplanted into a subject.

In one embodiment, contacting a cell with an iRNA includes "introducing" or "delivering the iRNA into the cell" by facilitating or effecting uptake or absorption into the cell. Absorption or uptake of an iRNA can occur through unaided diffusive or active cellular processes, or by auxiliary agents or devices. Introducing an iRNA into a cell may be *in vitro* and/or *in vivo*. For example, for *in vivo* introduction, iRNA can be injected into a tissue site or administered systemically. *In vivo* delivery can also be done by a beta-glucan delivery system. *In vitro* introduction into a cell includes methods known in the art such as electroporation and lipofection. Further approaches are described herein below and/or are known in the art.

The term "lipid nanoparticle" or "LNP" is a vesicle comprising a lipid layer encapsulating a pharmaceutically active molecule, such as a nucleic acid molecule, *e.g.*, an iRNA or a plasmid from which an iRNA is transcribed.

As used herein, a "subject" is an animal, such as a mammal, including a primate (such as a human, a non-human primate, *e.g.*, a monkey, and a chimpanzee), a non-primate (such as a cow, a pig, a camel, a llama, a horse, a goat, a rabbit, a sheep, a hamster, a guinea pig, a cat, a dog, a rat, a mouse, a horse, and a whale), or a bird (*e.g.*, a duck or a goose).

In an embodiment, the subject is a human, such as a human being treated or assessed for a disease, disorder or condition that would benefit from reduction in GRB14 expression; a human at risk for a disease, disorder or condition that would benefit from reduction in GRB14 expression; a human having a disease, disorder or condition that would benefit from reduction in GRB14 expression; and/or human being treated for a disease, disorder or condition that would benefit from reduction in GRB14 expression as described herein.

In another embodiment, the subject is homozygous for the GRB14 gene. Each allele of the gene may encode a functional GRB14 protein. In yet another embodiment, the subject is heterozygous for the GRB14 gene. The subject may have an allele encoding a functional GRB14 protein and an allele encoding a loss of

function variant of GRB14. In some embodiments, the subject has an allele encoding the rs3923113 variant. In some ebomdiments, the subject has an allele encoding the rs10195252 variant.

In some embodiments, the subject has a GIGYF1 loss of function allele. In some embodiments, the subject has a GIGYF1 rs221797 variant (e.g., rs221797:A). In some embodiments, the subject has a GIGYF1 rs117231629 variant. In some embodiments, the subject has a GIGYF2 loss of function allele. In some embodiments, the subject has a GIGYF2 rs1801251 variant (e.g., rs1801251:A).

As used herein, the terms "treating" or "treatment" refer to a beneficial or desired result including, but not limited to, alleviation or amelioration of one or more symptoms associated with GRB14 gene expression and/or GRB14 protein production. In some embodiments, symptoms associated with GRB14 gene expression and/or GRB14 protein production may be symptoms of a disease or disorder in which the pathology or cause is independent of GRB14 expression and/or GRB14 protein production, but which may nonetheless be compensated for/treated for/counteracted by inhibiting GRB14 gene expression and/or GRB14 protein production, *e.g.*, a GRB14-associated disease, such as type 2 diabetes, type 1 diabetes, prediabetes, insulin resistance, or a diabetes-related disease, disorder, or condition, such as obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc. "Treatment" can also mean prolonging survival as compared to expected survival in the absence of treatment.

The term "lower" in the context of a GRB14-associated disease refers to a statistically significant decrease in such level. The decrease can be, for example, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or more. In certain embodiments, a decrease is at least 20%. "Lower" in the context of the level of GRB14 in a subject is preferably down to a level accepted as within the range of normal for an individual without such disorder.

As used herein, "prevention" or "preventing," when used in reference to a disease, disorder or condition thereof, that would benefit from a reduction in expression of a GRB14 gene, refers to a reduction in the likelihood that a subject will develop a symptom associated with such disease, disorder, or condition, *e.g.*, a symptom of GRB14 gene expression or overexpression, such as insulin resistance. The failure to develop a disease, disorder or condition, or the reduction in the development of a symptom associated with such a disease, disorder or condition (*e.g.*, by at least about 10% on a clinically accepted scale for that disease or disorder), or the exhibition of delayed symptoms (*e.g.*, by days, weeks, months or years) is considered effective prevention.

As used herein, the terms and "GRB14-associated disease" are diseases or disorders that are caused by, or associated with, GRB14 gene expression, respectively, or by GRB14 protein production, respectively. The term "GRB14-associated disease" includes a disease, disorder or condition that would benefit from a

decrease in the gene expression or protein activity of GRB14, respectively. For instance, a "GRB14-associated disease" includes a disease or disorder which does not arise as a result of the expression of a GRB14 gene and/or production of a GRB14 protein, but in which the reduced expression of a GRB14 gene and/or production of a GRB14 protein may nonetheless alleviate the symptoms of or counteract or compensate for the adverse physiological effects of the disease or disorder. A subject having or being at risk for a GRB14-associated disease or disorder may include a subject expressing a wildtype GRB14 gene and/or otherwise exhibiting normal/healthy levels of expression of the GRB14 gene and levels of GRB14 protein production.

In one embodiment, a "GRB14-associated disease" is type 2 diabetes. In one embodiment, a "GRB14-associated disease" is type 1 diabetes. In one embodiment, a "GRB14-associated disease" is prediabetes. In one embodiment, a "GRB14-associated disease" is insulin resistance. In one embodiment, a "GRB14-associated disease" is a diabetes-related complication, such as obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc.

"Therapeutically effective amount," as used herein, is intended to include the amount of an RNAi agent that, when administered to a subject having a GRB14-associated disease, disorder, or condition, is sufficient to effective treatment of the disease (*e.g.*, by diminishing, ameliorating or maintaining the existing disease or one or more symptoms of disease). The "therapeutically effective amount" may vary depending on the RNAi agent, how the agent is administered, the disease and its severity and the history, age, weight, family history, genetic makeup, the types of preceding or concomitant treatments, if any, and other individual characteristics of the subject to be treated.

"Prophylactically effective amount," as used herein, is intended to include the amount of an iRNA that, when administered to a subject having a GRB14-associated disease, disorder, or condition, is sufficient to prevent or ameliorate the disease or one or more symptoms of the disease. Ameliorating the disease includes slowing the course of the disease or reducing the severity of later-developing disease. The "prophylactically effective amount" may vary depending on the iRNA, how the agent is administered, the degree of risk of disease, and the history, age, weight, family history, genetic makeup, the types of preceding or concomitant treatments, if any, and other individual characteristics of the patient to be treated.

A "therapeutically-effective amount" or "prophylactically effective amount" also includes an amount of an RNAi agent that produces some desired local or systemic effect at a reasonable benefit/risk ratio applicable to any treatment. iRNA employed in the methods of the present disclosure may be administered in a sufficient amount to produce a reasonable benefit/risk ratio applicable to such treatment.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in

contact with the tissues of human subjects and animal subjects without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The phrase "pharmaceutically-acceptable carrier" as used herein means a pharmaceutically-acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, manufacturing aid (*e.g.*, lubricant, talc magnesium, calcium or zinc stearate, or steric acid), or solvent encapsulating material, involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not injurious to the subject being treated. Some examples of materials which can serve as pharmaceutically-acceptable carriers include: (1) sugars, such as lactose, glucose and sucrose; (2) starches, such as corn starch and potato starch; (3) cellulose, and its derivatives, such as sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; (4) powdered tragacanth; (5) malt; (6) gelatin; (7) lubricating agents, such as magnesium state, sodium lauryl sulfate and talc; (8) excipients, such as cocoa butter and suppository waxes; (9) oils, such as peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; (10) glycols, such as propylene glycol; (11) polyols, such as glycerin, sorbitol, mannitol and polyethylene glycol; (12) esters, such as ethyl oleate and ethyl laurate; (13) agar; (14) buffering agents, such as magnesium hydroxide and aluminum hydroxide; (15) alginic acid; (16) pyrogen-free water; (17) isotonic saline; (18) Ringer's solution; (19) ethyl alcohol; (20) pH buffered solutions; (21) polyesters, polycarbonates and/or polyanhydrides; (22) bulking agents, such as polypeptides and amino acids (23) serum component, such as serum albumin, HDL and LDL; and (22) other non-toxic compatible substances employed in pharmaceutical formulations.

The term "sample," as used herein, includes a collection of similar fluids, cells, or tissues isolated from a subject, as well as fluids, cells, or tissues present within a subject. Examples of biological fluids include blood, serum and serosal fluids, plasma, cerebrospinal fluid, ocular fluids, lymph, urine, saliva, and the like. Tissue samples may include samples from tissues, organs or localized regions. For example, samples may be derived from particular organs, parts of organs, or fluids or cells within those organs. In certain embodiments, samples may be derived from the liver (*e.g.*, whole liver or certain segments of liver or certain types of cells in the liver, such as, *e.g.*, hepatocytes). In some embodiments, a "sample derived from a subject" refers to blood or plasma drawn from the subject.

II. iRNAs of the Disclosure

Described herein are iRNAs which inhibit the expression of a target gene. In one embodiment, the iRNAs inhibit the expression of a GRB14 gene. In one embodiment, the iRNA agent includes double stranded ribonucleic acid (dsRNA) molecules for inhibiting the expression of a GRB14 gene in a cell, such as a liver

cell, such as a liver cell within a subject, *e.g.*, a mammal, such as a human with type 2 diabetes, type 1 diabetes, prediabetes, or insulin resistance.

The dsRNA includes an antisense strand having a region of complementarity which is complementary to at least a part of an mRNA formed in the expression of a GRB14 gene. The region of complementarity is about 30 nucleotides or less in length (*e.g.*, about 30, 29, 28, 27, 26, 25, 24, 23, 22, 21, 20, 19, or 18 nucleotides or less in length). Upon contact with a cell expressing the target gene, the iRNA inhibits the expression of the target gene (*e.g.*, a human, a primate, a non-primate, or a bird target gene) by at least about 10% as assayed by, for example, a PCR or branched DNA (bDNA)-based method, or by a protein-based method, such as by immunofluorescence analysis, using, for example, Western Blotting or flow cytometric techniques.

A dsRNA includes two RNA strands that are complementary and hybridize to form a duplex structure under conditions in which the dsRNA will be used. One strand of a dsRNA (the antisense strand) includes a region of complementarity that is substantially complementary, and generally fully complementary, to a target sequence. The target sequence can be derived from the sequence of an mRNA formed during the expression of a GRB14 gene. The other strand (the sense strand) includes a region that is complementary to the antisense strand, such that the two strands hybridize and form a duplex structure when combined under suitable conditions. As described elsewhere herein and as known in the art, the complementary sequences of a dsRNA can also be contained as self-complementary regions of a single nucleic acid molecule, as opposed to being on separate oligonucleotides.

Generally, the duplex structure is between 15 and 30 base pairs in length, *e.g.*, between, 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 base pairs in length. Ranges and lengths intermediate to the above recited ranges and lengths are also contemplated to be part of the disclosure.

Similarly, the region of complementarity to the target sequence is between 15 and 30 nucleotides in length, *e.g.*, between 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 nucleotides in length. Ranges and lengths intermediate to the above recited ranges and lengths are also contemplated to be part of the disclosure.

In some embodiments, the sense and antisense strands of the dsRNA are each independently about 15 to about 30 nucleotides in length, or about 25 to about 30 nucleotides in length, *e.g.*, each strand is

independently between 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 nucleotides in length. In some embodiments, the dsRNA is between about 15 and about 23 nucleotides in length, or between about 25 and about 30 nucleotides in length. In general, the dsRNA is long enough to serve as a substrate for the Dicer enzyme. For example, it is well known in the art that dsRNAs longer than about 21-23 nucleotides can serve as substrates for Dicer. As the ordinarily skilled person will also recognize, the region of an RNA targeted for cleavage will most often be part of a larger RNA molecule, often an mRNA molecule. Where relevant, a "part" of an mRNA target is a contiguous sequence of an mRNA target of sufficient length to allow it to be a substrate for RNAi-directed cleavage (*i.e.*, cleavage through a RISC pathway).

One of skill in the art will also recognize that the duplex region is a primary functional portion of a dsRNA, *e.g.*, a duplex region of about 9 to 36 base pairs, *e.g.*, about 10-36, 11-36, 12-36, 13-36, 14-36, 15-36, 9-35, 10-35, 11-35, 12-35, 13-35, 14-35, 15-35, 9-34, 10-34, 11-34, 12-34, 13-34, 14-34, 15-34, 9-33, 10-33, 11-33, 12-33, 13-33, 14-33, 15-33, 9-32, 10-32, 11-32, 12-32, 13-32, 14-32, 15-32, 9-31, 10-31, 11-31, 12-31, 13-32, 14-31, 15-31, 15-30, 15-29, 15-28, 15-27, 15-26, 15-25, 15-24, 15-23, 15-22, 15-21, 15-20, 15-19, 15-18, 15-17, 18-30, 18-29, 18-28, 18-27, 18-26, 18-25, 18-24, 18-23, 18-22, 18-21, 18-20, 19-30, 19-29, 19-28, 19-27, 19-26, 19-25, 19-24, 19-23, 19-22, 19-21, 19-20, 20-30, 20-29, 20-28, 20-27, 20-26, 20-25, 20-24,20-23, 20-22, 20-21, 21-30, 21-29, 21-28, 21-27, 21-26, 21-25, 21-24, 21-23, or 21-22 base pairs. Thus, in one embodiment, to the extent that it becomes processed to a functional duplex, of *e.g.*, 15-30 base pairs, that targets a desired RNA for cleavage, an RNA molecule or complex of RNA molecules having a duplex region greater than 30 base pairs is a dsRNA. Thus, an ordinarily skilled artisan will recognize that in one embodiment, a miRNA is a dsRNA. In another embodiment, a dsRNA is not a naturally occurring miRNA. In another embodiment, an iRNA agent useful to target GRB14 expression is not generated in the target cell by cleavage of a larger dsRNA.

In one embodiment, the region of complementarity comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from nucleotides which are perfectly complementary to any 15 contiguous nucleotides positioned within nucleotides 166-188, 168-190, 169-191, 170-192, 171-193, 173-195, 174-196, 175-197, 180-202, 181-203, 182-204, 352-374, 353-375, 354-376, 355-377, 356-378, 358-380, 359-381, 360-382, 361-383, 362-384, 363-385, 364-386, 365-387, 366-388, 367-389, 368-390, 369-391, 370-392, 371-393, 373-395, 374-396, 375-397, 376-398, 377-399, 378-400, 379-401, 380-402, 381-403, 382-404, 383-405, 384-406, 385-407, 386-408, 387-409, 388-410, 389-411, 390-412, 391-413, 392-414, 393-415, 394-416, 395-417, 396-418, 397-419, 398-420, 399-421, 400-422, 401-423, 402-424, 403-425, 404-426, 405-427, 406-428, 407-429, 408-430409-431, 411-433, 412-434, 413-435, 414-436, 415-437, 416-438, 418-440, 419-441,

438-460, 439-461, 440-462, 441-463, 442-464, 464-486, 465-487, 466-488, 467-489, 468-490, 469-491, 470-492, 471-493, 472-494, 473-495, 474-496, 475-497, 476-498, 477-499, 478-500, 479-501, 480-502, 481-503, 482-504, 483-505, 484-506, 485-507, 486-508, 487-509, 506-528, 507-529, 508-530, 527-549, 528-550, 529-551, 530-552, 531-553, 532-554, 534-556, 535-557, 536-558, 537-559, 538-560, 540-562, 541-563, 542-564, 543-565, 545-567, 546-568, 548-570, 549-571, 550-572, 551-573, 552-574, 553-575, 554-576, 555-577, 556-578, 557-579, 558-580, 559-581, 560-582, 561-583, 562-584, 563-585, 564-586, 565-587, 566-588, 567-589, 568-590, 569-591, 570-592, 571-593, 572-594, 573-595, 574-596, 575-597, 576-598, 577-599, 578-600, 579-601, 580-602, 581-603, 582-604, 620-642, 621-643, 622-644, 628-650, 631-653, 636-658, 637-659, 638-660, 639-661, 640-662, 641-663, 642-664, 643-665, 644-666, 645-667, 646-668, 647-669, 648-670, 649-671, 650-672, 651-673, 652-674, 671-693, 672-694, 673-695, 674-696, 675-697, 676-698, 677-699, 678-700, 679-701, 680-702, 681-703, 682-704, 683-705, 736-758, 739-761, 740-762, 741-763, 742-764, 743-765, 744-766, 745-767, 746-768, 747-769, 748-770, 749-771, 750-772, 751-773, 752-774, 753-775, 754-776, 755-777, 756-778, 757-779, 758-780, 765-787, 766-788, 767-789, 768-790, 769-791, 770-792, 771-793, 772-794, 773-795, 774-796, 775-797, 776-798, 777-799, 778-800, 779-801, 780-802, 781-803, 782-804, 783-805, 784-806, 785-807, 786-808, 787-809, 788-810, 789-811, 790-812, 791-813, 792-814, 793-815, 793-815, 794-816, 795-817, 796-818, 797-819, 798-820, 798-820, 799-821, 800-822, 801-823, 844-866, 845-867, 846-868, 847-869, 848-870, 849-871, 850-872, 851-873, 852-874, 853-875, 872-894, 873-895, 874-896, 875-897, 876-898, 877-899, 878-900, 879-901, 880-902, 881-903, 882-904, 883-905, 884-906, 885-907, 886-908, 887-909, 888-910, 889-911, 890-912, 893-915, 894-916, 895-917, 896-918, 897-919, 898-920, 900-922, 901-923, 902-924,903-925, 904-926, 906-928, 907-929, 908-930, 909-931, 910-932, 911-933, 912-934, 913-935, 916-938, 917-939, 935-957, 936-958, 937-959, 938-960, 939-961, 940-962, 941-963, 942-964, 943-965, 944-966, 945-967, 948-970, 949-971, 951-973, 952-974, 957-979, 982-1004, 985-1007, 986-1008, 988-1010, 989-1011, 991-1013, 993-1015, 994-1016, 995-1017, 996-1018, 996-1018, 997-1019, 998-1020, 999-1021, 1000-1022, 1001-1023, 1002-1024, 1003-1025, 1004-1026, 1005-1027, 1006-1028, 1007-1029, 1008-1030, 1009-1031, 1010-1032, 1011-1033, 1012-1034, 1013-1035, 1014-1036, 1015-1037, 1016-1038, 1017-1039, 1019-1041, 1020-1042, 1021-1043, 1022-1044, 1023-1045, 1024-1046, 1061-1083, 1062-1084, 1063-1085, 1064-1086, 1065-1087, 1066-1088, 1067-1089, 1068-1090, 1069-1091, 1070-1092, 1071-1093, 1072-1094, 1073-1095, 1074-1096, 1075-1097, 1076-1098, 1077-1099, 1078-1100, 1079-1101, 1080-1102, 1081-1103, 1082-1104, 1083-1105, 1084-1106, 1085-1107, 1086-1108, 1087-1109, 1088-1110, 1089-1111, 1090-1112, 1120-1142, 1121-1143, 1122-1144, 1123-1145, 1124-1146, 1125-1147, 1126-1148, 1127-1149, 1128-1150, 1129-1151, 1130-1152, 1131-1153, 1132-1154, 1135-1157, 1136-1158, 1138-1160, 1139-1161, 1140-1162, 1141-1163, 1142-1164, 1143-1165, 1144-1166, 1149-1171, 1154-1176, 1155-1177, 1163-1185, 1164-1186, 1165-1187, 1167-1189, 1168-1190, 1169-1191, 1170-1192, 1171-1193, 1172-1194, 1173-1195, 1174-1196, 1175-1197, 1176-1198, 1177-1199, 1178-1200, 1179-1201, 1180-1202, 1181-1203, 1182-1204, 1183-1205, 1184-1206, 1185-1207, 1186-

1208, 1187-1209, 1188-1210, 1189-1211, 1191-1213, 1192-1214, 1196-1218, 1197-1219, 1198-1220, 1199-1221, 1201-1223, 1202-1224, 1203-1225, 1204-1226, 1205-1227, 1206-1228, 1207-1229, 1208-1230, 1209-1231, , 1210-1232, 1211-1233, 1212-1234, 1213-1235, 1214-1236, 1215-1237, 1216-1238, 1217-1239, 1218-1240, 1219-1241, 1220-1242, 1221-1243, 1222-1244, 1223-1245, 1224-1246, 1225-1247, 1226-1248, 1226-1248, 1227-1249, 1228-1250, 1247-1269, 1249-1271, 1250-1272, 1269-1291, 1270-1292, 1271-1293, 1272-1294, 1273-1295, 1296-1318, 1304-1326, 1307-1329, 1308-1330, 1309-1331, 1311-1333, 1316-1338, 1317-1339, 1318-1340, 1319-1341, 1320-1342, 1321-1343, 1322-1344, 1323-1345, 1324-1346, 1325-1347, 1326-1348, 1327-1349, 1328-1350, 1329-1351, 1330-1352, 1331-1353, 1332-1354, 1333-1355, 1334-1356, 1335-1357, 1336-1358, 1337-1359, 1339-1361, 1340-1362, 1341-1363, 1344-1366, 1345-1367, 1347-1369, 1348-1370, 1376-1398, 1377-1399, 1378-1400, 1379-1401, 1379-1401, 1380-1402, 1381-1403, 1382-1404, 1383-1405, 1384-1406, 1385-1407, 1386-1408, 1387-1409, 1388-1410, 1389-1411, 1390-1412, 1391-1413, 1392-1414, 1393-1415, 1394-1416, 1395-1417, 1407-1429, 1431-1453, 1451-1473, 1452-1474, 1453-1475, 1454-1476, 1455-1477, 1469-1491, 1470-1492, 1471-1493, 1471-1493, 1473-1495, 1476-1498, 1477-1499, 1478-1500, 1479-1501, 1480-1502, 1481-1503, 1482-1504, 1483-1505, 1484-1506, 1485-1507, 1486-1508, 1487-1509, 1488-1510, 1489-1511, 1490-1512, 1491-1513, 1492-1514, 1493-1515, 1494-1516, 1495-1517, 1496-1518, 1497-1519, 1498-1520, 1499-1521, 1500-1522, 1501-1523, 1506-1528, 1507-1529, 1510-1532, 1511-1533, 1512-1534, 1513-1535, 1514-1536, 1515-1537, 1516-1538, 1517-1539, 1518-1540, , 1519-1541, 1520-1542, 1521-1543, 1522-1544, 1523-1545, 1524-1546, 1525-1547, 1526-1548, 1527-1549, 1528-1550, 1529-1551, 1530-1552, 1531-1553, 1532-1554, 1536-1558, 1537-1559, 1539-1561, 1540-1562, 1541-1563, 1542-1564, 1543-1565, 1544-1566, 1545-1567, 1546-1568, 1547-1569, 1548-1570, 1549-1571, 1550-1572, 1551-1573, 1553-1575, 1554-1576, 1555-1577, 1556-1578, 1557-1579, 1558-1580, 1559-1581, 1560-1582, 1561-1583, 1562-1584, 1563-1585, 1564-1586, 1565-1587, 1566-1588, 1587-1609, 1588-1610, 1589-1611, 1590-1612, 1591-1613, 1592-1614, 1593-1615, 1594-1616, 1595-1617, 1596-1618, 1597-1619, 1598-1620, 1599-1621, 1600-1622, 1601-1623, 1602-1624, 1603-1625, 1604-1626, 1605-1627, 1606-1628, 1607-1629, 1608-1630, 1609-1631, 1610-1632, 1611-1633, 1612-1634, 1613-1635, 1614-1636, 1615-1637, 1616-1638, 1617-1639, 1618-1640, 1626-1648, 1627-1649, 1628-1650, 1629-1651, 1630-1652, 1631-1653, 1632-1654, 1633-1655, 1634-1656, 1635-1657, 1636-1658, 1637-1659, 1638-1660, 1639-1661, 1640-1662, 1641-1663, 1643-1665, 1644-1666, 1645-1667, 1646-1668, 1647-1669, 1648-1670, 1649-1671, 1650-1672, 1651-1673, 1652-1674, 1653-1675, 1654-1676, 1655-1677, 1656-1678, 1657-1679, 1658-1680, 1659-1681, 1660-1682, 1661-1683, 1663-1685, 1664-1686, 1665-1687, 1666-1688, 1667-1689, 1668-1690, 1689-1711, 1690-1712, 1691-1713, 1692-1714, 1693-1715, 1694-1716, 1695-1717, 1696-1718, 1715-1737, 1716-1738, 1717-1739, 1718-1740, 1719-1741, 1720-1742, 1721-1743, 1722-1744, 1723-1745, 1724-1746, 1725-1747, 1726-1748, 1727-1749, 1729-1751, 1730-1752, 1731-1753, 1732-1754, 1733-1755, 1734-1756, 1735-1757, 1736-1758, 1737-1759, 1738-1760, 1741-1763, 1744-1766, 1745-1767, 1746-1768, 1747-1769, 1748-1770, 1749-1771, 1750-

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2023, 2002-2024, 2003-2025, 2004-2026, 2005-2027, 2006-2028, 2007-2029, 2008-2030, 2009-2031, 2010-2032, 2011-2033, 2012-2034, 2013-2035, 2014-2036, 2015-2037, 2016-2038, 2017-2039, 2018-2040, 2019-2041, 2020-2042, 2021-2043, 2022-2044, 2023-2045, 2024-2046, 2025-2047, 2026-2048, 2027-2049, 2028-2050, 2029-2051, 2030-2052, 2031-2053, 2032-2054, 2033-2055, 2034-2056, 2070-2092, 2071-2093, 2072-2094, 2073-2095, 2074-2096, 2075-2097, 2076-2098, 2077-2099, 2078-2100, 2079-2101, 2080-2102, 2081-2103, 2082-2104, 2083-2105, 2084-2106, 2086-2108, 2117-2139, 2118-2140, 2129-2151, 2131-2153, 2133-2155, 2134-2156, 2135-2157, 2136-2158, 2137-2159, 2138-2160, 2139-2161, 2140-2162, 2141-2163, 2142-2164, 2143-2165, 2144-2166, 2145-2167, 2146-2168, 2147-2169, 2148-2170, 2149-2171, 2150-2172, 2151-2173, 2170-2192, 2226-2248, 2227-2249, 2228-2250, 2229-2251, 2230-2252, 2231-2253, 2232-2254, 2233-2255, 2234-2256, 2235-2257, 2236-2258, 2237-2259, 2238-2260, 2239-2261, 2240-2262, 2241-2263, 2242-2264, 2243-2265, 2244-2266, 2245-2267, 2246-2268, 2247-2269, 2248-2270, 2249-2271, 2250-2272, 2251-2273, 2293-2315, 2294-2316, 2316-2338, 2317-2339, 2338-2360, 2352-2374, 2354-2376, 2355-2377, 2356-2378, 2357-2379, 2358-2380, 1271-1293, 1272-1294, 1272-1294, 1316-1338, 1317-1339, 1320-1342, 1323-1345, 1325-1347, 1335-1357, 1379-1401, 1379-1401, 1384-1406, 1386-1408, 1387-1409, 1390-1412, 1391-1413, 1392-1414, 1394-1416, 1486-1508, 1487-1509, 1489-1511, 1595-1617, 1645-1667, 1650-1672, 1651-1673, 1729-1751, 1731-1753, 1741-1763, 1748-1770, 1748-1770, 1749-1771, 1751-1773, 1752-1774, 1754-1776, 1756-1778, 1760-1782, 1762-1784, 1768-1790, 1770-1792, 1770-1792, 1771-1793, 1772-1794, 1774-1796, 1800-1822, 1801-1823, 1827-1849, 1830-1852, 1881-1903, 1882-1904, 1902-1924, 1903-1925, 1916-1938, 1935-1957, 1937-1959, 1938-1960, 1940-1962, 1942-1964, 1943-1965, 1944-1966, 1945-1967, 1946-1968, 1947-1969, 1948-1970, 1949-1971, 1950-1972, 1951-1973, 1952-1974, 1955-1977, 1956-1978, 1957-1979, 869-891, 870-892, 871-893, 1710-1732, 1713-1735, 1825-1847, 1898-1920, 747-769, 784-806, 787-809, 788-810, 848-870, 848-870, 850-872, 852-874, 872-894, 877-899, 881-903, 882-904, 908-930, 910-932, 911-933, 912-934, 916-938, , 917-939, 989-1011, 989-1011, 996-1018, 996-1018, 998-1020, 1000-1022, 1008-1030, 1015-1037, 1020-1042, 1021-1043, 1022-1044, 1062-1084, 1076-1098, 1202-1224, 1206-1228, 1207-1229, 1208-1230, 1211-1233, 1947-1969, 1952-1974, 1956-1978, 1957-1979, 871-893, or 1756-1778 of SEQ ID NO: 1.

A dsRNA as described herein can further include one or more single-stranded nucleotide overhangs *e.g.,* 1, 2, 3, or 4 nucleotides. dsRNAs having at least one nucleotide overhang can have unexpectedly superior inhibitory properties relative to their blunt-ended counterparts. A nucleotide overhang can comprise or consist of a nucleotide/nucleoside analog, including a deoxynucleotide/nucleoside. The overhang(s) can be on the sense strand, the antisense strand or any combination thereof. Furthermore, the nucleotide(s) of an overhang can be present on the 5'-end, 3'-end or both ends of either an antisense or sense strand of a dsRNA.

A dsRNA can be synthesized by standard methods known in the art as further discussed below, *e.g.*, by use of an automated DNA synthesizer, such as are commercially available from, for example, Biosearch, Applied Biosystems, Inc.

iRNA compounds of the disclosure may be prepared using a two-step procedure. First, the individual strands of the double-stranded RNA molecule are prepared separately. Then, the component strands are annealed. The individual strands of the siRNA compound can be prepared using solution-phase or solid-phase organic synthesis or both. Organic synthesis offers the advantage that the oligonucleotide strands comprising unnatural or modified nucleotides can be easily prepared. Single-stranded oligonucleotides of the disclosure can be prepared using solution-phase or solid-phase organic synthesis or both.

In one aspect, a dsRNA of the disclosure includes at least two nucleotide sequences, a sense sequence and an anti-sense sequence. The sense strand sequence is selected from the group of sequences provided in Tables 2-7 or 15-16, and the corresponding nucleotide sequence of the antisense strand of the sense strand is selected from the group of sequences of any one of Tables 2-7 or 15-16. In this aspect, one of the two sequences is complementary to the other of the two sequences, with one of the sequences being substantially complementary to a sequence of an mRNA generated in the expression of a GRB14 gene. As such, in this aspect, a dsRNA will include two oligonucleotides, where one oligonucleotide is described as the sense strand (passenger strand) in Tables 2-7 or 15-16, and the second oligonucleotide is described as the corresponding antisense strand (guide strand) of the sense strand in Tables 2-7 or 15-16. In one embodiment, the substantially complementary sequences of the dsRNA are contained on separate oligonucleotides. In another embodiment, the substantially complementary sequences of the dsRNA are contained on a single oligonucleotide.

It will be understood that, although the sequences in Tables 2-7 or 15-16are described as modified, unmodified, unconjugated. and/or conjugated sequences, the RNA of the iRNA of the disclosure *e.g.*, a dsRNA of the disclosure, may comprise any one of the sequences set forth in Tables 2-7 or 15-16that is un-modified, un-conjugated, and/or modified and/or conjugated differently than described therein.

The skilled person is well aware that dsRNAs having a duplex structure of between about 20 and 23 base pairs, *e.g.,* 21, base pairs have been hailed as particularly effective in inducing RNA interference (Elbashir *et al.*, (2001) *EMBO J.*, 20:6877-6888). However, others have found that shorter or longer RNA duplex structures can also be effective (Chu and Rana (2007) *RNA* 14:1714-1719; Kim *et al.* (2005) *Nat Biotech* 23:222-226). In the embodiments described above, by virtue of the nature of the oligonucleotide sequences provided herein, dsRNAs described herein can include at least one strand of a length of minimally 21 nucleotides. It can be reasonably expected that shorter duplexes minus only a few nucleotides on one or both ends can be similarly effective as compared to the dsRNAs described above. Hence, dsRNAs having a sequence of at least 15, 16, 17, 18, 19, 20, or more contiguous nucleotides derived from one of the sequences provided herein, and differing in their ability to inhibit the expression of a GRB14 gene by not more than

about 5, 10, 15, 20, 25, or 30 % inhibition from a dsRNA comprising the full sequence, are contemplated to be within the scope of the present disclosure.

In addition, the RNAs described in Tables 2-7 or 15-16identify a site(s) in a GRB14 transcript that is susceptible to RISC-mediated cleavage. As such, the present disclosure further features iRNAs that target within these sites. As used herein, an iRNA is said to target within a particular site of an RNA transcript if the iRNA promotes cleavage of the transcript anywhere within that particular site. Such an iRNA will generally include at least about 15 contiguous nucleotides from one of the sequences provided herein coupled to additional nucleotide sequences taken from the region contiguous to the selected sequence in the gene.

While a target sequence is generally about 15-30 nucleotides in length, there is wide variation in the suitability of particular sequences in this range for directing cleavage of any given target RNA. Various software packages and the guidelines set out herein provide guidance for the identification of optimal target sequences for any given gene target, but an empirical approach can also be taken in which a "window" or "mask" of a given size (as a non-limiting example, 21 nucleotides) is literally or figuratively (including, *e.g.*, in silico) placed on the target RNA sequence to identify sequences in the size range that can serve as target sequences. By moving the sequence "window" progressively one nucleotide upstream or downstream of an initial target sequence location, the next potential target sequence can be identified, until the complete set of possible sequences is identified for any given target size selected. This process, coupled with systematic synthesis and testing of the identified sequences (using assays as described herein or as known in the art) to identify those sequences that perform optimally can identify those RNA sequences that, when targeted with an iRNA agent, mediate the best inhibition of target gene expression. Thus, while the sequences identified herein represent effective target sequences, it is contemplated that further optimization of inhibition efficiency can be achieved by progressively "walking the window" one nucleotide upstream or downstream of the given sequences to identify sequences with equal or better inhibition characteristics.

Further, it is contemplated that for any sequence identified herein, further optimization could be achieved by systematically either adding or removing nucleotides to generate longer or shorter sequences and testing those sequences generated by walking a window of the longer or shorter size up or down the target RNA from that point. Again, coupling this approach to generating new candidate targets with testing for effectiveness of iRNAs based on those target sequences in an inhibition assay as known in the art and/or as described herein can lead to further improvements in the efficiency of inhibition. Further still, such optimized sequences can be adjusted by, *e.g.*, the introduction of modified nucleotides as described herein or as known in the art, addition or changes in overhang, or other modifications as known in the art and/or discussed herein to further optimize the molecule (*e.g.*, increasing serum stability or circulating half-life, increasing thermal stability, enhancing transmembrane delivery, targeting to a particular location or cell type, increasing interaction with silencing pathway enzymes, increasing release from endosomes) as an expression inhibitor.

An iRNA agent as described herein can contain one or more mismatches to the target sequence. In one embodiment, an iRNA as described herein contains no more than 3 mismatches. If the antisense strand of the iRNA contains mismatches to a target sequence, it is preferable that the area of mismatch is not located in the center of the region of complementarity. If the antisense strand of the iRNA contains mismatches to the target sequence, it is preferable that the mismatch be restricted to be within the last 5 nucleotides from either the 5'- or 3'-end of the region of complementarity. For example, for a 23 nucleotide iRNA agent the strand which is complementary to a region of a GRB14 gene, generally does not contain any mismatch within the central 13 nucleotides. The methods described herein or methods known in the art can be used to determine whether an iRNA containing a mismatch to a target sequence is effective in inhibiting the expression of a GRB14 gene. Consideration of the efficacy of iRNAs with mismatches in inhibiting expression of a GRB14 gene is important, especially if the particular region of complementarity in a GRB14 gene is known to have polymorphic sequence variation within the population.

An RNA target may have regions, or spans of the target RNA's nucleotide sequence, which are relatively more susceptible or amenable than other regions of the RNA target to mediating cleavage of the RNA target via RNA interference induced by the binding of an RNAi agent to that region. The increased susceptibility to RNA interference within such "hotspot regions" (or simply "hotspots") means that iRNA agents targeting the region will likely have higher efficacy in inducing iRNA interference than iRNA agents which target other regions of the target RNA. For example, without being bound by theory, the accessibility of a target region of a target RNA may influence the efficacy of iRNA agents which target that region, with some hotspot regions having increased accessibility. Secondary structures, for instance, that form in the RNA target (e.g., within or proximate to hotspot regions) may affect the ability of the iRNA agent to bind the target region and induce RNA interference.

According to certain aspects of the disclosure, an iRNA agent may be designed to target a hotspot region of any of the target RNAs described herein, including any identified portions of a target RNA (e.g., a particular exon). As used herein, a hotspot region may refer to an approximately 19-200, 19-150, 19-100, 19-75, 19-50, 21-200, 21-150, 21-100, 21-75, 21-50, 50-200, 50-150, 50-100, 50-75, 75-200, 75-150, 75-100, 100-200, or 100-150 nucleotide region of a target RNA sequence for which targeting using RNAi agents provides an observably higher probability of efficacious silencing relative to targeting other regions of the same target RNA. According to certain aspects of the disclosure, a hotspot region may comprise a limited region of the target RNA, and in some cases, a substantially limited region of the target, including for example, less than half of the length of the target RNA, such as about 5%, 10%, 15%, 20%, 25%, or 30% of the length of the target RNA. Conversely, the other regions against which a hotspot is compared may cumulatively comprise at least a majority of the length of the target RNA. For example,

the other regions may cumulatively comprise at least about 60%, or at least about 70%, or at least about 80%, or at least about 90%, or at least about 95% of the length of the target RNA.

Compared regions of the target RNA may be empirically evaluated for identification of hotspots using efficacy data obtained from *in vitro* or *in vivo* screening assays. For example, RNAi agents targeting various regions that span a target RNA may be compared for frequency of efficacious iRNA agents (e.g., the amount by which target gene expression is inhibited, such as measured by mRNA expression or protein expression) that bind each region. In general, a hotspot can be recognized by observing clustering of multiple efficacious RNAi agents that bind to a limited region of the RNA target. A hotspot may be sufficiently characterized as such by observing efficacy of iRNA agents which cumulatively span at least about 60% of the target region identified as a hotspot, such as about 70%, about 80%, about 90%, or about 95% or more of the length of the region, including both ends of the region (i.e. at least about 60%, 70%, 80%, 90%, or 95% or more of the nucleotides within the region, including the nucleotides at each end of the region, were targeted by an iRNA agent). According to some aspects of the disclosure, an iRNA agent which demonstrates at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% inhibition over the region (e.g., no more than about 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, or 5% mRNA remaining) may be identified as efficacious.

Amenability to targeting of RNA regions may also be assessed using quantitative comparison of inhibition measurements across different regions of a defined size (e.g., 25, 30, 40, 50, 60, 70, 80, 90, or 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 nts). For example, an average level of inhibition may be determined for each region and the averages of each region may be compared. The average level of inhibition within a hotspot region may be substantially higher than the average of averages for all evaluated regions. According to some aspects, the average level of inhibition in a hotspot region may be at least about 10%, 20%, 30%, 40%, or 50% higher than the average of averages. According to some aspects, the average level of inhibition in a hotspot region may be at least about 1.0, 1.1, 1.2, 1.3, 1.4, 1.5 1.6, 1.7, 1.8. 1.9, or 2.0 standard deviations above the average of averages. The average level of inhibition may be higher by a statistically significant (e.g., $p < 0.05$) amount. According to some aspects, each inhibition measurement within a hotspot region may be above a threshold amount (e.g., at or below a threshold amount of mRNA remaining). According to some aspects, each inhibition measurement within the region may be substantially higher than an average of all inhibition measurements across all the measured regions. For example, each inhibition measurement in a hotspot region may be at least about 10%, 20%, 30%, 40%, or 50% higher than the average of all inhibition measurements. According to some aspects, each inhibition measurement may be at least about 1.0, 1.1, 1.2, 1.3, 1.4, 1.5 1.6, 1.7, 1.8. 1.9, or 2.0 standard deviations above the average of all inhibition measurements. Each inhibition measurement may be higher by a statistically significant (e.g., $p < 0.05$) amount than the average of all inhibition

measurements. A standard for evaluating a hotspot may comprise various combinations of the above standards where compatible (e.g., an average level of inhibition of at least about a first amount and having no inhibition measurements below a threshold level of a second amount, lesser than the first amount).

It is therefore expressly contemplated that any iRNA agent, including the specific exemplary iRNA agents described herein, which targets a hotspot region of a target RNA, may be preferably selected for inducing RNA interference of the target mRNA as targeting such a hotspot region is likely to exhibit a robust inhibitory response relative to targeting a region which is not a hotspot region. RNAi agents targeting target sequences that substantially overlap (e.g., by at least about 70%, 75%, 80%, 85%, 90%, 95% of the target sequence length) or, preferably, that reside fully within the hotspot region may be considered to target the hotspot region. Hotspot regions of the RNA target(s) of the instant disclosure may include any region for which the data disclosed herein demonstrates higher frequency of targeting by efficacious RNAi agents, including by any of the standards described elsewhere herein, whether or not the range(s) of such hotspot region(s) are explicitly specified.

In various embodiments, a dsRNA agent of the present disclosure targets a hotspot region of an mRNA encoding GRB14. In one aspect, the present disclosure provides a dsRNA agent that targets a hotspot region of a GRB14 mRNA.

III. Modified iRNAs of the Disclosure

In one embodiment, the RNA of the iRNA of the disclosure *e.g.*, a dsRNA, is un-modified, and does not comprise, *e.g.,* chemical modifications and/or conjugations known in the art and described herein. In another embodiment, the RNA of an iRNA of the disclosure, *e.g.*, a dsRNA, is chemically modified to enhance stability or other beneficial characteristics. In certain embodiments of the disclosure, substantially all of the nucleotides of an iRNA of the disclosure are modified. In other embodiments of the disclosure, all of the nucleotides of an iRNA of the disclosure are modified. iRNAs of the disclosure in which "substantially all of the nucleotides are modified" are largely but not wholly modified and can include not more than 5, 4, 3, 2, or 1 unmodified nucleotides.

In some aspects of the disclosure, substantially all of the nucleotides of an iRNA of the disclosure are modified and the iRNA agents comprise no more than 10 nucleotides comprising 2`-fluoro modifications (*e.g.*, no more than 9 2′-fluoro modifications, no more than 8 2′-fluoro modifications, no more than 7 2′-fluoro modifications, no more than 6 2′-fluoro modifications, no more than 5 2′-fluoro modifications, no more than 4 2′-fluoro modifications, no more than 5 2′-fluoro modifications, no more than 4 2′-fluoro modifications, no more than 3 2′-fluoro modifications, or no more than 2 2′-fluoro modifications). For example, in some embodiments, the sense strand comprises no more than 4 nucleotides comprising 2′-fluoro modifications (*e.g.*, no more than 3 2′-fluoro modifications, or no more than 2 2′-fluoro modifications). In other embodiments, the

antisense strand comprises no more than 6 nucleotides comprising 2′-fluoro modifications (*e.g.*, no more than 5 2′-fluoro modifications, no more than 4 2′-fluoro modifications, no more than 4 2′-fluoro modifications, or no more than 2 2′-fluoro modifications).

In other aspects of the disclosure, all of the nucleotides of an iRNA of the disclosure are modified and the iRNA agents comprise no more than 10 nucleotides comprising 2'-fluoro modifications (*e.g.*, no more than 9 2′-fluoro modifications, no more than 8 2′-fluoro modifications, no more than 7 2′-fluoro modifications, no more than 6 2′-fluoro modifications, no more than 5 2′-fluoro modifications, no more than 4 2′-fluoro modifications, no more than 5 2′-fluoro modifications, no more than 4 2′-fluoro modifications, no more than 3 2′-fluoro modifications, or no more than 2 2′-fluoro modifications).

In one embodiment, the double stranded RNAi agent of the disclosure further comprises a 5'-phosphate or a 5'-phosphate mimic at the 5' nucleotide of the antisense strand. In another embodiment, the double stranded RNAi agent further comprises a 5'-phosphate or 5'-phosphate mimic at the 5' nucleotide of the sense strand. In a specific embodiment, the 5'-phosphate mimic is a 5'-vinylphosphonate (5'-VP).

The nucleic acids featured in the disclosure can be synthesized and/or modified by methods well established in the art, such as those described in "Current protocols in nucleic acid chemistry," Beaucage, S.L. *et al.* (Edrs.), John Wiley & Sons, Inc., New York, NY, USA, which is hereby incorporated herein by reference. Modifications include, for example, end modifications, *e.g.*, 5'-end modifications (phosphorylation, conjugation, inverted linkages) or 3'-end modifications (conjugation, DNA nucleotides, inverted linkages, *etc.*); base modifications, *e.g.*, replacement with stabilizing bases, destabilizing bases, or bases that base pair with an expanded repertoire of partners, removal of bases (abasic nucleotides), or conjugated bases; sugar modifications (*e.g.*, at the 2'-position or 4'-position) or replacement of the sugar; and/or backbone modifications, including modification or replacement of the phosphodiester linkages. Specific examples of iRNA compounds useful in the embodiments described herein include, but are not limited to RNAs containing modified backbones or no natural internucleoside linkages. RNAs having modified backbones include, among others, those that do not have a phosphorus atom in the backbone. For the purposes of this specification, and as sometimes referenced in the art, modified RNAs that do not have a phosphorus atom in their internucleoside backbone can also be considered to be oligonucleosides. In some embodiments, a modified iRNA will have a phosphorus atom in its internucleoside backbone.

Modified RNA backbones include, for example, phosphorothioates, chiral phosphorothioates, phosphorodithioates, phosphotriesters, aminoalkylphosphotriesters, methyl and other alkyl phosphonates including 3'-alkylene phosphonates and chiral phosphonates, phosphinates, phosphoramidates including 3'-amino phosphoramidate and aminoalkylphosphoramidates, thionophosphoramidates, thionoalkylphosphonates, thionoalkylphosphotriesters, and boranophosphates having normal 3'-5' linkages, 2'-5'-linked analogs of these, and those having inverted polarity wherein the adjacent pairs of nucleoside units are linked 3'-5' to 5'-3' or 2'-5'

to 5'-2'. Various salts, mixed salts and free acid forms are also included. In some embodiments of the disclosure, the dsRNA agents of the disclosure are in a free acid form. In other embodiments of the disclosure, the dsRNA agents of the disclosure are in a salt form. In one embodiment, the dsRNA agents of the disclosure are in a sodium salt form. In certain embodiments, when the dsRNA agents of the disclosure are in the sodium salt form, sodium ions are present in the agent as counterions for substantially all of the phosphodiester and/or phosphorothioate groups present in the agent. Agents in which substantially all of the phosphodiester and/or phosphorothioate linkages have a sodium counterion include not more than 5, 4, 3, 2, or 1 phosphodiester and/or phosphorothioate linkages without a sodium counterion. In some embodiments, when the dsRNA agents of the disclosure are in the sodium salt form, sodium ions are present in the agent as counterions for all of the phosphodiester and/or phosphorothioate groups present in the agent.

Representative U.S. patents that teach the preparation of the above phosphorus-containing linkages include, but are not limited to, U.S. Patent Nos. 3,687,808; 4,469,863; 4,476,301; 5,023,243; 5,177,195; 5,188,897; 5,264,423; 5,276,019; 5,278,302; 5,286,717; 5,321,131; 5,399,676; 5,405,939; 5,453,496; 5,455,233; 5,466,677; 5,476,925; 5,519,126; 5,536,821; 5,541,316; 5,550,111; 5,563,253; 5,571,799; 5,587,361; 5,625,050; 6,028,188; 6,124,445; 6,160,109; 6,169,170; 6,172,209; 6, 239,265; 6,277,603; 6,326,199; 6,346,614; 6,444,423; 6,531,590; 6,534,639; 6,608,035; 6,683,167; 6,858,715; 6,867,294; 6,878,805; 7,015,315; 7,041,816; 7,273,933; 7,321,029; and US Pat RE39464, the entire contents of each of which are hereby incorporated herein by reference.

Modified RNA backbones that do not include a phosphorus atom therein have backbones that are formed by short chain alkyl or cycloalkyl internucleoside linkages, mixed heteroatoms and alkyl or cycloalkyl internucleoside linkages, or one or more short chain heteroatomic or heterocyclic internucleoside linkages. These include those having morpholino linkages (formed in part from the sugar portion of a nucleoside); siloxane backbones; sulfide, sulfoxide and sulfone backbones; formacetyl and thioformacetyl backbones; methylene formacetyl and thioformacetyl backbones; alkene containing backbones; sulfamate backbones; methyleneimino and methylenehydrazino backbones; sulfonate and sulfonamide backbones; amide backbones; and others having mixed N, O, S and CH_2 component parts.

Representative U.S. patents that teach the preparation of the above oligonucleosides include, but are not limited to, U.S. Patent Nos. 5,034,506; 5,166,315; 5,185,444; 5,214,134; 5,216,141; 5,235,033; 5,64,562; 5,264,564; 5,405,938; 5,434,257; 5,466,677; 5,470,967; 5,489,677; 5,541,307; 5,561,225; 5,596,086; 5,602,240; 5,608,046; 5,610,289; 5,618,704; 5,623,070; 5,663,312; 5,633,360; 5,677,437; and, 5,677,439, the entire contents of each of which are hereby incorporated herein by reference.

In other embodiments, suitable RNA mimetics are contemplated for use in iRNAs, in which both the sugar and the internucleoside linkage, *i.e.*, the backbone, of the nucleotide units are replaced with novel groups. The base units are maintained for hybridization with an appropriate nucleic acid target compound.

One such oligomeric compound, an RNA mimetic that has been shown to have excellent hybridization properties, is referred to as a peptide nucleic acid (PNA). In PNA compounds, the sugar backbone of an RNA is replaced with an amide containing backbone, in particular an aminoethylglycine backbone. The nucleobases are retained and are bound directly or indirectly to aza nitrogen atoms of the amide portion of the backbone. Representative U.S. patents that teach the preparation of PNA compounds include, but are not limited to, U.S. Patent Nos. 5,539,082; 5,714,331; and 5,719,262, the entire contents of each of which are hereby incorporated herein by reference. Additional PNA compounds suitable for use in the iRNAs of the disclosure are described in, for example, in Nielsen *et al.*, *Science*, 1991, 254, 1497-1500.

Some embodiments featured in the disclosure include RNAs with phosphorothioate backbones and oligonucleosides with heteroatom backbones, and in particular --CH_2--NH--CH_2-, --CH_2--N(CH_3)--O--CH_2-- [known as a methylene (methylimino) or MMI backbone], --CH_2--O--N(CH_3)--CH_2--, --CH_2--N(CH_3)--N(CH_3)--CH_2-- and --N(CH_3)--CH_2----[wherein the native phosphodiester backbone is represented as --O--P--O--CH_2--] of the above-referenced U.S. Patent No. 5,489,677, and the amide backbones of the above-referenced U.S. Patent No. 5,602,240. In some embodiments, the RNAs featured herein have morpholino backbone structures of the above-referenced U.S. Patent No. 5,034,506.

Modified RNAs can also contain one or more substituted sugar moieties. The iRNAs, *e.g.*, dsRNAs, featured herein can include one of the following at the 2'-position: OH; F; O-, S-, or N-alkyl; O-, S-, or N-alkenyl; O-, S- or N-alkynyl; or O-alkyl-O-alkyl, wherein the alkyl, alkenyl and alkynyl can be substituted or unsubstituted C_1 to C_{10} alkyl or C_2 to C_{10} alkenyl and alkynyl. Exemplary suitable modifications include $O[(CH_2)_nO]_mCH_3$, $O(CH_2)_nOCH_3$, $O(CH_2)_nNH_2$, $O(CH_2)_nCH_3$, $O(CH_2)_nONH_2$, and $O(CH_2)_nON[(CH_2)_nCH_3)]_2$, where n and m are from 1 to about 10. In other embodiments, dsRNAs include one of the following at the 2' position: C_1 to C_{10} lower alkyl, substituted lower alkyl, alkaryl, aralkyl, O-alkaryl or O-aralkyl, SH, SCH_3, OCN, Cl, Br, CN, CF_3, OCF_3, $SOCH_3$, SO_2CH_3, ONO_2, NO_2, N_3, NH_2, heterocycloalkyl, heterocycloalkaryl, aminoalkylamino, polyalkylamino, substituted silyl, an RNA cleaving group, a reporter group, an intercalator, a group for improving the pharmacokinetic properties of an iRNA, or a group for improving the pharmacodynamic properties of an iRNA, and other substituents having similar properties. In some embodiments, the modification includes a 2'-methoxyethoxy (2'-O--$CH_2CH_2OCH_3$, also known as 2'-O-(2-methoxyethyl) or 2'-MOE) (Martin *et al.*, *Helv. Chim. Acta*, 1995, 78:486-504) *i.e.*, an alkoxy-alkoxy group. Another exemplary modification is 2'-dimethylaminooxyethoxy, *i.e.*, a $O(CH_2)_2ON(CH_3)_2$ group, also known as 2'-DMAOE, as described in examples herein below, and 2'-dimethylaminoethoxyethoxy (also known in the art as 2'-O-dimethylaminoethoxyethyl or 2'-DMAEOE), *i.e.*, 2'-O--CH_2--O--CH_2--N(CH_2)$_2$. Further exemplary modifications include: 5'-Me-2'-F nucleotides, 5'-Me-2'-OMe nucleotides, 5'-Me-2'-deoxynucleotides, (both R and S isomers in these three families); 2'-alkoxyalkyl; and 2'-NMA (N-methylacetamide).

Other modifications include 2'-methoxy (2'-OCH_3), 2'-aminopropoxy (2'-$OCH_2CH_2CH_2NH_2$) and 2'-fluoro (2'-F). Similar modifications can also be made at other positions on the RNA of an iRNA, particularly the 3' position of the sugar on the 3' terminal nucleotide or in 2'-5' linked dsRNAs and the 5' position of 5' terminal nucleotide. iRNAs can also have sugar mimetics such as cyclobutyl moieties in place of the pentofuranosyl sugar. Representative U.S. patents that teach the preparation of such modified sugar structures include, but are not limited to, U.S. Pat. Nos. 4,981,957; 5,118,800; 5,319,080; 5,359,044; 5,393,878; 5,446,137; 5,466,786; 5,514,785; 5,519,134; 5,567,811; 5,576,427; 5,591,722; 5,597,909; 5,610,300; 5,627,053; 5,639,873; 5,646,265; 5,658,873; 5,670,633; and 5,700,920, certain of which are commonly owned with the instant application. The entire contents of each of the foregoing are hereby incorporated herein by reference.

An iRNA of the disclosure can also include nucleobase (often referred to in the art simply as "base") modifications or substitutions. As used herein, "unmodified" or "natural" nucleobases include the purine bases adenine (A) and guanine (G), and the pyrimidine bases thymine (T), cytosine (C) and uracil (U). Modified nucleobases include other synthetic and natural nucleobases such as 5-methylcytosine (5-me-C), 5-hydroxymethyl cytosine, xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 2-thiouracil, 2-thiothymine and 2-thiocytosine, 5-halouracil and cytosine, 5-propynyl uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudouracil), 4-thiouracil, 8-halo, 8-amino, 8-thiol, 8-thioalkyl, 8-hydroxyl anal other 8-substituted adenines and guanines, 5-halo, particularly 5-bromo, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine and 7-methyladenine, 8-azaguanine and 8-azaadenine, 7-deazaguanine and 7-daazaadenine and 3-deazaguanine and 3-deazaadenine. Further nucleobases include those disclosed in U.S. Pat. No. 3,687,808, those disclosed in Modified Nucleosides in Biochemistry, Biotechnology and Medicine, Herdewijn, P. ed. Wiley-VCH, 2008; those disclosed in The Concise Encyclopedia Of Polymer Science And Engineering, pages 858-859, Kroschwitz, J. L, ed. John Wiley & Sons, 1990, these disclosed by Englisch *et al.*, (1991) *Angewandte Chemie, International Edition*, 30:613, and those disclosed by Sanghvi, Y S., Chapter 15, dsRNA Research and Applications, pages 289-302, Crooke, S. T. and Lebleu, B., Ed., CRC Press, 1993. Certain of these nucleobases are particularly useful for increasing the binding affinity of the oligomeric compounds featured in the disclosure. These include 5-substituted pyrimidines, 6-azapyrimidines and N-2, N-6 and 0-6 substituted purines, including 2-aminopropyladenine, 5-propynyluracil and 5-propynylcytosine. 5-methylcytosine substitutions have been shown to increase nucleic acid duplex stability by 0.6-1.2 °C (Sanghvi, Y. S., Crooke, S. T. and Lebleu, B., Eds., dsRNA Research and Applications, CRC Press, Boca Raton, 1993, pp. 276-278) and are exemplary base substitutions, even more particularly when combined with 2'-O-methoxyethyl sugar modifications.

Representative U.S. patents that teach the preparation of certain of the above noted modified nucleobases as well as other modified nucleobases include, but are not limited to, the above noted U.S. Patent Nos. 3,687,808, 4,845,205; 5,130,30; 5,134,066; 5,175,273; 5,367,066; 5,432,272; 5,457,187; 5,459,255; 5,484,908; 5,502,177; 5,525,711; 5,552,540; 5,587,469; 5,594,121, 5,596,091; 5,614,617; 5,681,941; 5,750,692; 6,015,886; 6,147,200; 6,166,197; 6,222,025; 6,235,887; 6,380,368; 6,528,640; 6,639,062; 6,617,438; 7,045,610; 7,427,672; and 7,495,088, the entire contents of each of which are hereby incorporated herein by reference.

An iRNA of the disclosure can also be modified to include one or more locked nucleic acids (LNA). A locked nucleic acid is a nucleotide having a modified ribose moiety in which the ribose moiety comprises an extra bridge connecting the 2' and 4' carbons. This structure effectively "locks" the ribose in the 3'-endo structural conformation. The addition of locked nucleic acids to siRNAs has been shown to increase siRNA stability in serum, and to reduce off-target effects (Elmen, J. *et al.*, (2005) *Nucleic Acids Research* 33(1):439-447; Mook, OR. *et al.*, (2007) *Mol Canc Ther* 6(3):833-843; Grunweller, A. *et al.*, (2003) *Nucleic Acids Research* 31(12):3185-3193).

An iRNA of the disclosure can also be modified to include one or more bicyclic sugar moieties. A "bicyclic sugar" is a furanosyl ring modified by the bridging of two atoms. A "bicyclic nucleoside" ("BNA") is a nucleoside having a sugar moiety comprising a bridge connecting two carbon atoms of the sugar ring, thereby forming a bicyclic ring system. In certain embodiments, the bridge connects the 4'-carbon and the 2'-carbon of the sugar ring. Thus, in some embodiments an agent of the disclosure may include one or more locked nucleic acids (LNA). A locked nucleic acid is a nucleotide having a modified ribose moiety in which the ribose moiety comprises an extra bridge connecting the 2' and 4' carbons. In other words, an LNA is a nucleotide comprising a bicyclic sugar moiety comprising a 4'-CH2-O-2' bridge. This structure effectively "locks" the ribose in the 3'-endo structural conformation. The addition of locked nucleic acids to siRNAs has been shown to increase siRNA stability in serum, and to reduce off-target effects (Elmen, J. *et al.*, (2005) *Nucleic Acids Research* 33(1):439-447; Mook, OR. *et al.*, (2007) *Mol Canc Ther* 6(3):833-843; Grunweller, A. *et al.*, (2003) *Nucleic Acids Research* 31(12):3185-3193). Examples of bicyclic nucleosides for use in the polynucleotides of the disclosure include without limitation nucleosides comprising a bridge between the 4' and the 2' ribosyl ring atoms. In certain embodiments, the antisense polynucleotide agents of the disclosure include one or more bicyclic nucleosides comprising a 4' to 2' bridge. Examples of such 4' to 2' bridged bicyclic nucleosides, include but are not limited to 4'-(CH2)—O-2' (LNA); 4'-(CH2)—S-2'; 4'-(CH2)2—O-2' (ENA); 4'-CH(CH3)—O-2' (also referred to as "constrained ethyl" or "cEt") and 4'-CH(CH2OCH3)—O-2' (and analogs thereof; see, *e.g.*, U.S. Pat. No. 7,399,845); 4'-C(CH3)(CH3)—O-2' (and analogs thereof; see *e.g.*, US Patent No. 8,278,283); 4'-CH2—N(OCH3)-2' (and analogs thereof; see *e.g.*, US Patent No. 8,278,425); 4'-CH2—O—N(CH3)-2' (see, e.g., U.S. Patent Publication No. 2004/0171570); 4'-CH2—

N(R)—O-2', wherein R is H, C1-C12 alkyl, or a protecting group (see, *e.g.*, U.S. Pat. No. 7,427,672); 4'-CH2—C(H)(CH3)-2' (see, *e.g.*, Chattopadhyaya *et al., J. Org. Chem.*, 2009, 74, 118-134); and 4'-CH2—C(=CH2)-2' (and analogs thereof; see, *e.g.*, US Patent No. 8,278,426). The entire contents of each of the foregoing are hereby incorporated herein by reference.

Additional representative U.S. Patents and US Patent Publications that teach the preparation of locked nucleic acid nucleotides include, but are not limited to, the following: U.S. Patent Nos. 6,268,490; 6,525,191; 6,670,461; 6,770,748; 6,794,499; 6,998,484; 7,053,207; 7,034,133;7,084,125; 7,399,845; 7,427,672; 7,569,686; 7,741,457; 8,022,193; 8,030,467; 8,278,425; 8,278,426; 8,278,283; US 2008/0039618; and US 2009/0012281, the entire contents of each of which are hereby incorporated herein by reference.

Any of the foregoing bicyclic nucleosides can be prepared having one or more stereochemical sugar configurations including for example α-L-ribofuranose and β-D-ribofuranose (see WO 99/14226).

An iRNA of the disclosure can also be modified to include one or more constrained ethyl nucleotides. As used herein, a "constrained ethyl nucleotide" or "cEt" is a locked nucleic acid comprising a bicyclic sugar moiety comprising a 4'-CH(CH3)-0-2' bridge. In one embodiment, a constrained ethyl nucleotide is in the S conformation referred to herein as "S-cEt."

An iRNA of the disclosure may also include one or more "conformationally restricted nucleotides" ("CRN"). CRN are nucleotide analogs with a linker connecting the C2'and C4' carbons of ribose or the C3 and -C5' carbons of ribose. CRN lock the ribose ring into a stable conformation and increase the hybridization affinity to mRNA. The linker is of sufficient length to place the oxygen in an optimal position for stability and affinity resulting in less ribose ring puckering.

Representative publications that teach the preparation of certain of the above noted CRN include, but are not limited to, US Patent Publication No. 2013/0190383; and PCT publication WO 2013/036868, the entire contents of each of which are hereby incorporated herein by reference.

In some embodiments, an iRNA of the disclosure comprises one or more monomers that are UNA (unlocked nucleic acid) nucleotides. UNA is unlocked acyclic nucleic acid, wherein any of the bonds of the sugar has been removed, forming an unlocked "sugar" residue. In one example, UNA also encompasses monomer with bonds between C1'-C4' have been removed (i.e. the covalent carbon-oxygen-carbon bond between the C1' and C4' carbons). In another example, the C2'-C3' bond (i.e. the covalent carbon-carbon bond between the C2' and C3' carbons) of the sugar has been removed (see *Nuc. Acids Symp. Series,* 52, 133-134 (2008) and Fluiter et al., *Mol. Biosyst.,* 2009, 10, 1039 hereby incorporated by reference).

Representative U.S. publications that teach the preparation of UNA include, but are not limited to, US Patent No. 8,314,227; and US Patent Publication Nos. 2013/0096289; 2013/0011922; and 2011/0313020, the entire contents of each of which are hereby incorporated herein by reference.

Potentially stabilizing modifications to the ends of RNA molecules can include N-(acetylaminocaproyl)-4-hydroxyprolinol (Hyp-C6-NHAc), N-(caproyl-4-hydroxyprolinol (Hyp-C6), N-(acetyl-4-hydroxyprolinol (Hyp-NHAc), thymidine-2'-0-deoxythymidine (ether), N-(aminocaproyl)-4-hydroxyprolinol (Hyp-C6-amino), 2-docosanoyl-uridine-3"- phosphate, inverted base dT(idT) and others. Disclosure of this modification can be found in PCT Publication No. WO 2011/005861.

Other modifications of an iRNA of the disclosure include a 5' phosphate or 5' phosphate mimic, *e.g.*, a 5'-terminal phosphate or phosphate mimic on the antisense strand of an RNAi agent. Suitable phosphate mimics are disclosed in, for example US Patent Publication No. 2012/0157511, the entire contents of which are incorporated herein by reference.

In certain specific embodiments, an RNAi agent of the present disclosure is an agent that inhibits the expression of a GRB14 gene which is selected from the group of agents listed in Tables 2-7 or 15-16. Any of these agents may further comprise a ligand.

A. Modified iRNAs Comprising Motifs of the Disclosure

In certain aspects of the disclosure, the double stranded RNAi agents of the disclosure include agents with chemical modifications as disclosed, for example, in WO 2013/075035, filed on November 16, 2012, the entire contents of which are incorporated herein by reference. The RNAi agent may be optionally conjugated with a GalNAc ligand, for instance on the sense strand.

Accordingly, the disclosure provides double stranded RNAi agents capable of inhibiting the expression of a target gene (*i.e.*, a GRB14 gene) *in vivo*. The RNAi agent comprises a sense strand and an antisense strand. Each strand of the RNAi agent may range from 12-30 nucleotides in length. For example, each strand may be between 14-30 nucleotides in length, 17-30 nucleotides in length, 25-30 nucleotides in length, 27-30 nucleotides in length, 17-23 nucleotides in length, 17-21 nucleotides in length, 17-19 nucleotides in length, 19-25 nucleotides in length, 19-23 nucleotides in length, 19-21 nucleotides in length, 21-25 nucleotides in length, or 21-23 nucleotides in length. In one embodiment, the sense strand is 21 nulceotides in length. In one embodiment, the antisense strand is 23 nucleotides in length.

The sense strand and antisense strand typically form a duplex double stranded RNA ("dsRNA"), also referred to herein as an "RNAi agent." The duplex region of an RNAi agent may be 12-30 nucleotide pairs in length. For example, the duplex region can be between 14-30 nucleotide pairs in length, 17-30 nucleotide pairs in length, 27-30 nucleotide pairs in length, 17 - 23 nucleotide pairs in length, 17-21 nucleotide pairs in length, 17-19 nucleotide pairs in length, 19-25 nucleotide pairs in length, 19-23 nucleotide pairs in length, 19- 21 nucleotide pairs in length, 21-25 nucleotide pairs in length, or 21-23 nucleotide pairs in length. In another example, the duplex region is selected from 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, and 27 nucleotides in length.

In one embodiment, the RNAi agent may contain one or more overhang regions and/or capping groups at the 3'-end, 5'-end, or both ends of one or both strands. The overhang can be 1-6 nucleotides in length, for instance 2-6 nucleotides in length, 1-5 nucleotides in length, 2-5 nucleotides in length, 1-4 nucleotides in length, 2-4 nucleotides in length, 1-3 nucleotides in length, 2-3 nucleotides in length, or 1-2 nucleotides in length. The overhangs can be the result of one strand being longer than the other, or the result of two strands of the same length being staggered. The overhang can form a mismatch with the target mRNA or it can be complementary to the gene sequences being targeted or can be another sequence. The first and second strands can also be joined, *e.g.*, by additional bases to form a hairpin, or by other non-base linkers.

In one embodiment, the nucleotides in the overhang region of the RNAi agent can each independently be a modified or unmodified nucleotide including, but no limited to 2'-sugar modified, such as, 2-F, 2'-Omethyl, thymidine (T), 2'-O-methoxyethyl-5-methyluridine (Teo), 2'-O-methoxyethyladenosine (Aeo), 2'-O-methoxyethyl-5-methylcytidine (m5Ceo), and any combinations thereof. For example, TT can be an overhang sequence for either end on either strand. The overhang can form a mismatch with the target mRNA or it can be complementary to the gene sequences being targeted or can be another sequence.

The 5'- or 3'- overhangs at the sense strand, antisense strand or both strands of the RNAi agent may be phosphorylated. In some embodiments, the overhang region(s) contains two nucleotides having a phosphorothioate between the two nucleotides, where the two nucleotides can be the same or different. In one embodiment, the overhang is present at the 3'-end of the sense strand, antisense strand, or both strands. In one embodiment, this 3'-overhang is present in the antisense strand. In one embodiment, this 3'-overhang is present in the sense strand.

The RNAi agent may contain only a single overhang, which can strengthen the interference activity of the RNAi, without affecting its overall stability. For example, the single-stranded overhang may be located at the 3'-terminal end of the sense strand or, alternatively, at the 3'-terminal end of the antisense strand. The RNAi may also have a blunt end, located at the 5'-end of the antisense strand (or the 3'-end of the sense strand) or *vice versa*. Generally, the antisense strand of the RNAi has a nucleotide overhang at the 3'-end, and the 5'-end is blunt. While not wishing to be bound by theory, the asymmetric blunt end at the 5'-end of the antisense strand and 3'-end overhang of the antisense strand favor the guide strand loading into RISC process.

In one embodiment, the RNAi agent is a double ended bluntmer of 19 nucleotides in length, wherein the sense strand contains at least one motif of three 2'-F modifications on three consecutive nucleotides at positions 7, 8, 9 from the 5'end. The antisense strand contains at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at positions 11, 12, 13 from the 5'end.

In another embodiment, the RNAi agent is a double ended bluntmer of 20 nucleotides in length, wherein the sense strand contains at least one motif of three 2'-F modifications on three consecutive

nucleotides at positions 8, 9, 10 from the 5'end. The antisense strand contains at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at positions 11, 12, 13 from the 5'end.

In yet another embodiment, the RNAi agent is a double ended bluntmer of 21 nucleotides in length, wherein the sense strand contains at least one motif of three 2'-F modifications on three consecutive nucleotides at positions 9, 10, 11 from the 5'end. The antisense strand contains at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at positions 11, 12, 13 from the 5'end.

In one embodiment, the RNAi agent comprises a 21 nucleotide sense strand and a 23 nucleotide antisense strand, wherein the sense strand contains at least one motif of three 2'-F modifications on three consecutive nucleotides at positions 9, 10, 11 from the 5'end; the antisense strand contains at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at positions 11, 12, 13 from the 5'end, wherein one end of the RNAi agent is blunt, while the other end comprises a 2 nucleotide overhang. Preferably, the 2 nucleotide overhang is at the 3'-end of the antisense strand.

When the 2 nucleotide overhang is at the 3'-end of the antisense strand, there may be two phosphorothioate internucleotide linkages between the terminal three nucleotides, wherein two of the three nucleotides are the overhang nucleotides, and the third nucleotide is a paired nucleotide next to the overhang nucleotide. In one embodiment, the RNAi agent additionally has two phosphorothioate internucleotide linkages between the terminal three nucleotides at both the 5'-end of the sense strand and at the 5'-end of the antisense strand. In one embodiment, every nucleotide in the sense strand and the antisense strand of the RNAi agent, including the nucleotides that are part of the motifs are modified nucleotides. In one embodiment each residue is independently modified with a 2'-O-methyl or 3'-fluoro, *e.g.,* in an alternating motif. Optionally, the RNAi agent further comprises a ligand ($GalNAc_3$).

In one embodiment, the RNAi agent comprises a sense and an antisense strand, wherein the sense strand is 25-30 nucleotide residues in length, wherein starting from the 5' terminal nucleotide (position 1) positions 1 to 23 of the first strand comprise at least 8 ribonucleotides; the antisense strand is 36-66 nucleotide residues in length and, starting from the 3' terminal nucleotide, comprises at least 8 ribonucleotides in the positions paired with positions 1- 23 of sense strand to form a duplex; wherein at least the 3 ' terminal nucleotide of antisense strand is unpaired with sense strand, and up to 6 consecutive 3' terminal nucleotides are unpaired with sense strand, thereby forming a 3' single stranded overhang of 1-6 nucleotides; wherein the 5' terminus of antisense strand comprises from 10-30 consecutive nucleotides which are unpaired with sense strand, thereby forming a 10-30 nucleotide single stranded 5' overhang; wherein at least the sense strand 5' terminal and 3' terminal nucleotides are base paired with nucleotides of antisense strand when sense and antisense strands are aligned for maximum complementarity, thereby forming a substantially duplexed region between sense and antisense strands; and antisense strand is sufficiently complementary to a target RNA along at least 19 ribonucleotides of antisense strand length to reduce target gene expression when the double

stranded nucleic acid is introduced into a mammalian cell; and wherein the sense strand contains at least one motif of three 2'-F modifications on three consecutive nucleotides, where at least one of the motifs occurs at or near the cleavage site. The antisense strand contains at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at or near the cleavage site.

In one embodiment, the RNAi agent comprises sense and antisense strands, wherein the RNAi agent comprises a first strand having a length which is at least 25 and at most 29 nucleotides and a second strand having a length which is at most 30 nucleotides with at least one motif of three 2'-O-methyl modifications on three consecutive nucleotides at position 11, 12, 13 from the 5' end; wherein the 3' end of the first strand and the 5' end of the second strand form a blunt end and the second strand is 1-4 nucleotides longer at its 3' end than the first strand, wherein the duplex region which is at least 25 nucleotides in length, and the second strand is sufficiently complementary to a target mRNA along at least 19 nucleotide of the second strand length to reduce target gene expression when the RNAi agent is introduced into a mammalian cell, and wherein dicer cleavage of the RNAi agent preferentially results in an siRNA comprising the 3' end of the second strand, thereby reducing expression of the target gene in the mammal. Optionally, the RNAi agent further comprises a ligand.

In one embodiment, the sense strand of the RNAi agent contains at least one motif of three identical modifications on three consecutive nucleotides, where one of the motifs occurs at the cleavage site in the sense strand.

In one embodiment, the antisense strand of the RNAi agent can also contain at least one motif of three identical modifications on three consecutive nucleotides, where one of the motifs occurs at or near the cleavage site in the antisense strand.

For an RNAi agent having a duplex region of 17-23 nucleotide in length, the cleavage site of the antisense strand is typically around the 10, 11 and 12 positions from the 5'-end. Thus the motifs of three identical modifications may occur at the 9, 10, 11 positions; 10, 11, 12 positions; 11, 12, 13 positions; 12, 13, 14 positions; or 13, 14, 15 positions of the antisense strand, the count starting from the 1st nucleotide from the 5'-end of the antisense strand, or, the count starting from the 1st paired nucleotide within the duplex region from the 5'- end of the antisense strand. The cleavage site in the antisense strand may also change according to the length of the duplex region of the RNAi from the 5'-end.

The sense strand of the RNAi agent may contain at least one motif of three identical modifications on three consecutive nucleotides at the cleavage site of the strand; and the antisense strand may have at least one motif of three identical modifications on three consecutive nucleotides at or near the cleavage site of the strand. When the sense strand and the antisense strand form a dsRNA duplex, the sense strand and the antisense strand can be so aligned that one motif of the three nucleotides on the sense strand and one motif of the three nucleotides on the antisense strand have at least one nucleotide overlap, *i.e.*, at least one of the three

nucleotides of the motif in the sense strand forms a base pair with at least one of the three nucleotides of the motif in the antisense strand. Alternatively, at least two nucleotides may overlap, or all three nucleotides may overlap.

In one embodiment, the sense strand of the RNAi agent may contain more than one motif of three identical modifications on three consecutive nucleotides. The first motif may occur at or near the cleavage site of the strand and the other motifs may be a wing modification. The term "wing modification" herein refers to a motif occurring at another portion of the strand that is separated from the motif at or near the cleavage site of the same strand. The wing modification is either adjacent to the first motif or is separated by at least one or more nucleotides. When the motifs are immediately adjacent to each other, then the chemistry of the motifs are distinct from each other and when the motifs are separated by one or more nucleotide than the chemistries can be the same or different. Two or more wing modifications may be present. For instance, when two wing modifications are present, each wing modification may occur at one end relative to the first motif which is at or near cleavage site or on either side of the lead motif.

Like the sense strand, the antisense strand of the RNAi agent may contain more than one motifs of three identical modifications on three consecutive nucleotides, with at least one of the motifs occurring at or near the cleavage site of the strand. This antisense strand may also contain one or more wing modifications in an alignment similar to the wing modifications that may be present on the sense strand.

In one embodiment, the wing modification on the sense strand or antisense strand of the RNAi agent typically does not include the first one or two terminal nucleotides at the 3'-end, 5'-end or both ends of the strand.

In another embodiment, the wing modification on the sense strand or antisense strand of the RNAi agent typically does not include the first one or two paired nucleotides within the duplex region at the 3'-end, 5'-end or both ends of the strand.

When the sense strand and the antisense strand of the RNAi agent each contain at least one wing modification, the wing modifications may fall on the same end of the duplex region, and have an overlap of one, two or three nucleotides.

When the sense strand and the antisense strand of the RNAi agent each contain at least two wing modifications, the sense strand and the antisense strand can be so aligned that two modifications each from one strand fall on one end of the duplex region, having an overlap of one, two or three nucleotides; two modifications each from one strand fall on the other end of the duplex region, having an overlap of one, two or three nucleotides; two modifications one strand fall on each side of the lead motif, having an overlap of one, two or three nucleotides in the duplex region.

In one embodiment, every nucleotide in the sense strand and antisense strand of the RNAi agent, including the nucleotides that are part of the motifs, may be modified. Each nucleotide may be modified with

the same or different modification which can include one or more alteration of one or both of the non-linking phosphate oxygens and/or of one or more of the linking phosphate oxygens; alteration of a constituent of the ribose sugar, *e.g.*, of the 2′ hydroxyl on the ribose sugar; wholesale replacement of the phosphate moiety with "dephospho" linkers; modification or replacement of a naturally occurring base; and replacement or modification of the ribose-phosphate backbone.

As nucleic acids are polymers of subunits, many of the modifications occur at a position which is repeated within a nucleic acid, *e.g.*, a modification of a base, or a phosphate moiety, or a non-linking O of a phosphate moiety. In some cases, the modification will occur at all of the subject positions in the nucleic acid but in many cases it will not. By way of example, a modification may only occur at a 3' or 5' terminal position, may only occur in a terminal region, *e.g.*, at a position on a terminal nucleotide or in the last 2, 3, 4, 5, or 10 nucleotides of a strand. A modification may occur in a double strand region, a single strand region, or in both. A modification may occur only in the double strand region of a RNA or may only occur in a single strand region of a RNA. For example, a phosphorothioate modification at a non-linking O position may only occur at one or both termini, may only occur in a terminal region, *e.g.*, at a position on a terminal nucleotide or in the last 2, 3, 4, 5, or 10 nucleotides of a strand, or may occur in double strand and single strand regions, particularly at termini. The 5' end or ends can be phosphorylated.

It may be possible, *e.g.*, to enhance stability, to include particular bases in overhangs, or to include modified nucleotides or nucleotide surrogates, in single strand overhangs, *e.g.*, in a 5' or 3' overhang, or in both. For example, it can be desirable to include purine nucleotides in overhangs. In some embodiments all or some of the bases in a 3' or 5' overhang may be modified, *e.g.*, with a modification described herein. Modifications can include, *e.g.*, the use of modifications at the 2' position of the ribose sugar with modifications that are known in the art, *e.g.*, the use of deoxyribonucleotides, 2'-deoxy-2'-fluoro (2'-F) or 2'-O-methyl modified instead of the ribosugar of the nucleobase, and modifications in the phosphate group, *e.g.*, phosphorothioate modifications. Overhangs need not be homologous with the target sequence.

In one embodiment, each residue of the sense strand and antisense strand is independently modified with LNA, CRN, cET, UNA, HNA, CeNA, 2'-methoxyethyl, 2'- O-methyl, 2'-O-allyl, 2'-C- allyl, 2'-deoxy, or 2'-fluoro. The strands can contain more than one modification. In one embodiment, each residue of the sense strand and antisense strand is independently modified with 2'- O-methyl or 2'-fluoro. In one embodiment, each residue of the sense strand and antisense strand is independently modified with 2'- O-methyl, 2'-fluoro, and/or a deoxy-nucleotide.

At least two different modifications are typically present on the sense strand and antisense strand. Those two modifications may be the 2'- O-methyl or 2'-fluoro modifications, or others.

In one embodiment, the RNAi agent comprises the pattern of the alternating motif of 2'-O-methyl modification and 2'-F modification on the sense strand initially has a shift relative to the pattern of the

alternating motif of 2'-O-methyl modification and 2'-F modification on the antisense strand initially, *i.e.*, the 2'-O-methyl modified nucleotide on the sense strand base pairs with a 2'-F modified nucleotide on the antisense strand and vice versa. The 1 position of the sense strand may start with the 2'-F modification, and the 1 position of the antisense strand may start with the 2'- O-methyl modification.

The introduction of one or more motifs of three identical modifications on three consecutive nucleotides to the sense strand and/or antisense strand interrupts the initial modification pattern present in the sense strand and/or antisense strand. This interruption of the modification pattern of the sense and/or antisense strand by introducing one or more motifs of three identical modifications on three consecutive nucleotides to the sense and/or antisense strand surprisingly enhances the gene silencing activity to the target gene.

The RNAi agent may further comprise at least one phosphorothioate or methylphosphonate internucleotide linkage. The phosphorothioate or methylphosphonate internucleotide linkage modification may occur on any nucleotide of the sense strand or antisense strand or both strands in any position of the strand. For instance, the internucleotide linkage modification may occur on every nucleotide on the sense strand and/or antisense strand; each internucleotide linkage modification may occur in an alternating pattern on the sense strand and/or antisense strand; or the sense strand or antisense strand may contain both internucleotide linkage modifications in an alternating pattern. The alternating pattern of the internucleotide linkage modification on the sense strand may be the same or different from the antisense strand, and the alternating pattern of the internucleotide linkage modification on the sense strand may have a shift relative to the alternating pattern of the internucleotide linkage modification on the antisense strand. In one embodiment, a double-stranded RNAi agent comprises 6-8phosphorothioate internucleotide linkages. In one embodiment, the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and the sense strand comprises at least two phosphorothioate internucleotide linkages at either the 5'-terminus or the 3'-terminus.

In one embodiment, the RNAi comprises a phosphorothioate or methylphosphonate internucleotide linkage modification in the overhang region. For example, the overhang region may contain two nucleotides having a phosphorothioate or methylphosphonate internucleotide linkage between the two nucleotides. Internucleotide linkage modifications also may be made to link the overhang nucleotides with the terminal paired nucleotides within the duplex region. For example, at least 2, 3, 4, or all the overhang nucleotides may be linked through phosphorothioate or methylphosphonate internucleotide linkage, and optionally, there may be additional phosphorothioate or methylphosphonate internucleotide linkages linking the overhang nucleotide with a paired nucleotide that is next to the overhang nucleotide. For instance, there may be at least two phosphorothioate internucleotide linkages between the terminal three nucleotides, in which two of the three nucleotides are overhang nucleotides, and the third is a paired nucleotide next to the overhang nucleotide.

These terminal three nucleotides may be at the 3'-end of the antisense strand, the 3'-end of the sense strand, the 5'-end of the antisense strand, and/or the 5'end of the antisense strand.

In one embodiment, the 2 nucleotide overhang is at the 3'-end of the antisense strand, and there are two phosphorothioate internucleotide linkages between the terminal three nucleotides, wherein two of the three nucleotides are the overhang nucleotides, and the third nucleotide is a paired nucleotide next to the overhang nucleotide. Optionally, the RNAi agent may additionally have two phosphorothioate internucleotide linkages between the terminal three nucleotides at both the 5'-end of the sense strand and at the 5'-end of the antisense strand.

In one embodiment, the RNAi agent comprises mismatch(es) with the target, within the duplex, or combinations thereof. The mistmatch may occur in the overhang region or the duplex region. The base pair may be ranked on the basis of their propensity to promote dissociation or melting (*e.g.*, on the free energy of association or dissociation of a particular pairing, the simplest approach is to examine the pairs on an individual pair basis, though next neighbor or similar analysis can also be used). In terms of promoting dissociation: A:U is preferred over G:C; G:U is preferred over G:C; and I:C is preferred over G:C (I=inosine). Mismatches, *e.g.*, non-canonical or other than canonical pairings (as described elsewhere herein) are preferred over canonical (A:T, A:U, G:C) pairings; and pairings which include a universal base are preferred over canonical pairings.

In one embodiment, the RNAi agent comprises at least one of the first 1, 2, 3, 4, or 5 base pairs within the duplex regions from the 5'- end of the antisense strand independently selected from the group of: A:U, G:U, I:C, and mismatched pairs, *e.g.*, non-canonical or other than canonical pairings or pairings which include a universal base, to promote the dissociation of the antisense strand at the 5'-end of the duplex.

In one embodiment, the nucleotide at the 1 position within the duplex region from the 5'-end in the antisense strand is selected from the group consisting of A, dA, dU, U, and dT. Alternatively, at least one of the first 1, 2 or 3 base pair within the duplex region from the 5'- end of the antisense strand is an AU base pair. For example, the first base pair within the duplex region from the 5'- end of the antisense strand is an AU base pair.

In another embodiment, the nucleotide at the 3'-end of the sense strand is deoxy-thymine (dT). In another embodiment, the nucleotide at the 3'-end of the antisense strand is deoxy-thymine (dT). In one embodiment, there is a short sequence of deoxy-thymine nucleotides, for example, two dT nucleotides on the 3'-end of the sense and/or antisense strand.

In certain embodiments, an RNAi agent of the disclosure may contain a low number of nucleotides containing a 2'-fluoro modification, e.g., 10 or fewer nucleotides with 2'-fluoro modification. For example, the RNAi agent may contain 10, 9, 8, 7, 6, 5, 4, 3, 2, 1 or 0 nucleotides with a 2'-fluoro modification. In a specific embodiment, the RNAi agent of the disclosure contains 10 nucleotides with a 2'-fluoro modification,

e.g., 4 nucleotides with a 2'-fluoro modification in the sense strand and 6 nucleotides with a 2'-fluoro modification in the antisense strand. In another specific embodiment, the RNAi agent of the disclosure contains 6 nucleotides with a 2'-fluoro modification, e.g., 4 nucleotides with a 2'-fluoro modification in the sense strand and 2 nucleotides with a 2'-fluoro modification in the antisense strand.

In other embodiments, an RNAi agent of the disclosure may contain an ultra-low number of nucleotides containing a 2'-fluoro modification, e.g., 2 or fewer nucleotides containing a 2'-fluoro modification. For example, the RNAi agent may contain 2, 1 of 0 nucleotides with a 2'-fluoro modification. In a specific embodiment, the RNAi agent may contain 2 nucleotides with a 2'-fluoro modification, *e.g.*, 0 nucleotides with a 2-fluoro modification in the sense strand and 2 nucleotides with a 2'-fluoro modification in the antisense strand.

Various publications describe multimeric RNAi agents that can be used in the methods of the disclosure.

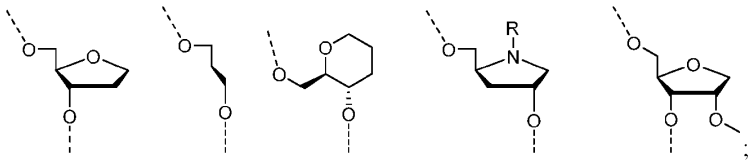
As described in more detail below, the RNAi agent that contains conjugations of one or more carbohydrate moieties to a RNAi agent can optimize one or more properties of the RNAi agent. In many cases, the carbohydrate moiety will be attached to a modified subunit of the RNAi agent. For example, the ribose sugar of one or more ribonucleotide subunits of a dsRNA agent can be replaced with another moiety, *e.g.*, a non-carbohydrate (preferably cyclic) carrier to which is attached a carbohydrate ligand. A ribonucleotide subunit in which the ribose sugar of the subunit has been so replaced is referred to herein as a ribose replacement modification subunit (RRMS). A cyclic carrier may be a carbocyclic ring system, *i.e.*, all ring atoms are carbon atoms, or a heterocyclic ring system, *i.e.*, one or more ring atoms may be a heteroatom, e.g., nitrogen, oxygen, sulfur. The cyclic carrier may be a monocyclic ring system, or may contain two or more rings, *e.g.* fused rings. The cyclic carrier may be a fully saturated ring system, or it may contain one or more double bonds.

The ligand may be attached to the polynucleotide via a carrier. The carriers include (i) at least one "backbone attachment point," preferably two "backbone attachment points" and (ii) at least one "tethering attachment point." A "backbone attachment point" as used herein refers to a functional group, e.g. a hydroxyl group, or generally, a bond available for, and that is suitable for incorporation of the carrier into the backbone, e.g., the phosphate, or modified phosphate, e.g., sulfur containing, backbone, of a ribonucleic acid. A "tethering attachment point" (TAP) in some embodiments refers to a constituent ring atom of the cyclic carrier, e.g., a carbon atom or a heteroatom (distinct from an atom which provides a backbone attachment point), that connects a selected moiety. The moiety can be, e.g., a carbohydrate, e.g. monosaccharide, disaccharide, trisaccharide, tetrasaccharide, oligosaccharide and polysaccharide. Optionally, the selected moiety is connected by an intervening tether to the cyclic carrier. Thus, the cyclic carrier will often include a

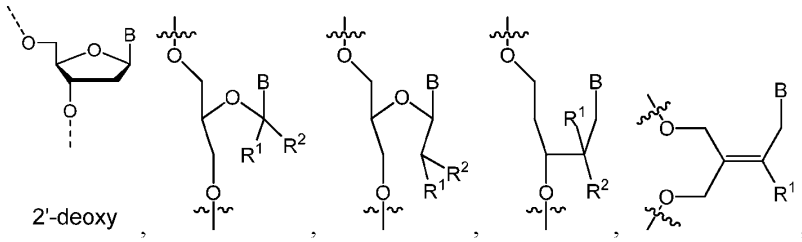
functional group, e.g., an amino group, or generally, provide a bond, that is suitable for incorporation or tethering of another chemical entity, *e.g.*, a ligand to the constituent ring.

The RNAi agents may be conjugated to a ligand *via* a carrier, wherein the carrier can be cyclic group or acyclic group; preferably, the cyclic group is selected from pyrrolidinyl, pyrazolinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, piperidinyl, piperazinyl, [1,3]dioxolane, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, quinoxalinyl, pyridazinonyl, tetrahydrofuryl and decalin; preferably, the acyclic group is selected from serinol backbone or diethanolamine backbone.

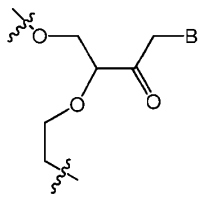
The RNAi agents may comprise a thermally destabilizing nucleotide placed at a site opposite to the seed region of the antisense strand (i.e., at positions 2-8 of the 5'-end of the antisense strand). For example, a thermally destabilizing nucleotide may be at a position of the sense strand that pairs with a nucleotide at positions 2-8 of the 5'-end of the antisense strand. In one example, a thermally destabilizing nucleotide is at position 15 from the 5'-end of the sense strand. A thermally destabilizing nucleotide nucleotide bears the thermally destabilizing modification which can include abasic modification; mismatch with the opposing nucleotide in the duplex; and sugar modification such as 2'-deoxy modification or acyclic nucleotide *e.g.*, unlocked nucleic acids (UNA) or glycerol nucleic acid (GNA). In certain embodiments, the thermally destabilizing modification selected from the group consisting of: i) mismatch with the opposing nucleotide in the antisense strand; ii) abasic modification selected from the group consisting of:



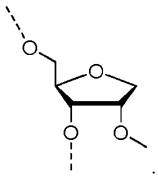
; and iii) sugar modification selected from the group consisting of:

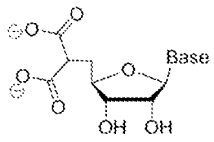


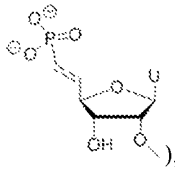
2'-deoxy , , , , , and

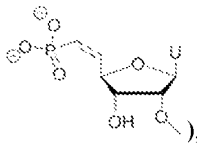


, wherein B is a modified or unmodified nucleobase, R^1 and R^2 independently are H,

halogen, OR_3, or alkyl; and R_3 is H, alkyl, cycloalkyl, aryl, aralkyl, heteroaryl or sugar. In certain embodiments, the thermally destabilizing modification is a mismatch selected from the group consisting of G:G, G:A, G:U, G:T, A:A, A:C, C:C, C:U, C:T, U:U, T:T, and U:T; and optionally, at least one nucleobase in the mismatch pair is a 2'-deoxy nucleobase. In one example, the thermally destabilizing modification is GNA or .

The RNAi agent can comprise a phosphorus-containing group at the 5'-end of the sense strand or antisense strand. The 5'-end phosphorus-containing group can be 5'-end phosphate (5'-P), 5'-end phosphorothioate (5'-PS), 5'-end phosphorodithioate (5'-PS_2), 5'-end vinylphosphonate (5'-VP), 5'-end methylphosphonate (MePhos), or 5'-deoxy-5'-*C*-malonyl (

). When the 5'-end phosphorus-containing group is 5'-end vinylphosphonate (5'-VP), the 5'-VP can be either 5'-*E*-VP isomer (i.e., *trans*-vinylphosphonate, 

), 5'-*Z*-VP isomer (i.e., *cis*-vinylphosphonate, 

), or mixtures thereof.

In certain embodiments, the RNAi agent comprises a phosphorus-containing group at the 5'-end of the sense strand. In certain embodiments, the RNAi agent comprises a phosphorus-containing group at the 5'-end of the antisense strand.

In certain embodiments, the RNAi agent comprises a 5'-P. In certain embodiments, the RNAi agent comprises a 5'-P in the antisense strand.

In certain embodiments, the RNAi agent comprises a 5'-PS. In certain embodiments, the RNAi agent comprises a 5'-PS in the antisense strand.

In certain embodiments, the RNAi agent comprises a 5'-VP. In certain embodiments, the RNAi agent comprises a 5'-VP in the antisense strand. In certain embodiments, the RNAi agent comprises a 5'-

E-VP in the antisense strand. In certain embodiments, the RNAi agent comprises a 5'-*Z*-VP in the antisense strand.

In certain embodiments, the RNAi agent comprises a 5'-PS_2. In certain embodiments, the RNAi agent comprises a 5'-PS_2 in the antisense strand.

In certain embodiments, the RNAi agent comprises a 5'-PS_2. In certain embodiments, the RNAi agent comprises a 5'-deoxy-5'-*C*-malonyl in the antisense strand.

In another embodiment, an RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an asialoglycoprotein receptor (ASGPR) ligand, and (iii) 2'-F modifications at positions 1, 3, 5, 7, 9 to 11, 13, 17, 19, and 21, and 2'-OMe modifications at positions 2, 4, 6, 8, 12, 14 to 16, 18, and 20 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 5, 9, 11 to 13, 15, 17, 19, 21, and 23, and 2'F modifications at positions 2, 4, 6 to 8, 10, 14, 16, 18, 20, and 22 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the dsRNA agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, an RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-F modifications at positions 1, 3, 5, 7, 9 to 11, 13, 15, 17, 19, and 21, and 2'-OMe modifications at positions 2, 4, 6, 8, 12, 14, 16, 18, and 20 (counting from the 5' end); and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 5, 7, 9, 11 to 13, 15, 17, 19, and 21 to 23, and 2'F modifications at positions 2, 4, 6, 8, 10, 14, 16, 18, and 20 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, an RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, 10, and 12 to 21, 2'-F modifications at positions 7 and 9, and a deoxy-nucleotide (*e.g.* dT) at position 11 (counting from the 5' end); and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 7, 9,

11, 13, 15, 17, and 19 to 23, and 2'-F modifications at positions 2, 4 to 6, 8, 10, 12, 14, 16, and 18 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, an RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, 10, 12, 14, and 16 to 21, and 2'-F modifications at positions 7, 9, 11, 13, and 15; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 5, 7, 9, 11, 13, 15, 17, 19, and 21 to 23, and 2'-F modifications at positions 2 to 4, 6, 8, 10, 12, 14, 16, 18, and 20 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, an RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 9, and 12 to 21, and 2'-F modifications at positions 10, and 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 5, 7, 9, 11 to 13, 15, 17, 19, and 21 to 23, and 2'-F modifications at positions 2, 4, 6, 8, 10, 14, 16, 18, and 20 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-F modifications at positions 1, 3, 5, 7, 9 to 11, and 13, and 2'-OMe modifications at positions 2, 4, 6, 8, 12, and 14 to 21; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 5 to 7, 9, 11 to 13, 15, 17 to 19, and 21 to 23, and

2'-F modifications at positions 2, 4, 8, 10, 14, 16, and 20 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii)an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, and 12 to 21, and 2'-F modifications at positions 7 and 9 to 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3 to 5, 7, 8, 10 to 13, 15, and 17 to 23, and 2'-F modifications at positions 2, 6, 9, 14, and 16 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, and 12 to 21, and 2'-F modifications at positions 7 and 9 to 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3 to 5, 7, 10 to 13, 15, and 17 to 23, and 2'-F modifications at positions 2, 6, 8, 9, 14, and 16 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 19 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 4, 6, and 10 to 19, and 2'-F modifications at positions 5 and 7 to 9; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 21 nucleotides; (ii) 2'-OMe modifications at positions 1, 3 to 5, 7, 10 to 13, 15, and 17 to 21, and 2'-F modifications at positions 2, 6, 8, 9, 14, and 16 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between

nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 19 and 20, and between nucleotide positions 20 and 21 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 8 and 12 to 21, and 2'-F modifications at positions 9 to 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3, 4, 6, 8 to 11, 13, 15 to 23, and a 2'-F modification at position 14, and 2'-deoxy-modified nucleotides at positions 2, 5, 7, and 12 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, and 12 to 21, and 2'-F modifications at positions 7 and 9 to 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3 to 4, 6, 8 to 13, 15, and 17 to 23, and 2'-F modifications at positions 2, 14, and 16, a 2'-deoxy-modified nucleotide at position 5, and a GNA at position 7 (counting from the 5' end); and (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In another embodiment, a RNAi agent of the present disclosure comprises: (a) a sense strand having: (i) a length of 21 nucleotides; (ii) an ASGPR ligand; (iii) 2'-OMe modifications at positions 1 to 6, 8, and 12 to 21, and 2'-F modifications at positions 7 and 9 to 11; and (iv) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2 and between nucleotide positions 2 and 3 (counting from the 5' end); and (b) an antisense strand having: (i) a length of 23 nucleotides; (ii) 2'-OMe modifications at positions 1, 3 to 5, 7 to 13, 15, and 17 to 23, and 2'-F modifications at positions 2, 6, 14, and 16 (counting from the 5' end) (iii) phosphorothioate internucleotide linkages between nucleotide positions 1 and 2, between nucleotide positions 2 and 3, between nucleotide positions 21 and 22, and

between nucleotide positions 22 and 23 (counting from the 5' end); wherein the RNAi agents have a two-nucleotide overhang at the 3'-end of the antisense strand, and a blunt end at the 5'-end of the antisense strand.

In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 7 and 9 to 11 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 9 to 11 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 7 to 9 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 5 and 7 to 9 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 9, 11, and 13 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 9, 11, and 12 (counting from the 5' end). In some embodiments, the sense strand of the RNAi agent has 2'-F modifications at positions 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 (counting from the 5' end).

In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 1, 2, 6, 14, and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 4, 6, 12, 14, 16, 18, and 19 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 3, 5, 10, 12, 14, and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 4, 12, 14 and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 12, 14, and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 6, 14, and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has 2'-F modifications at positions 2, 14, and 16 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has a 2'-F modification at only position 14 (counting from the 5' end).

In some embodiments, the antisense strand of the RNAi agent has 2'-deoxy-modified nucleotides at positions 2, 5, 7, and 12 (counting from the 5' end). In some embodiments, the antisense strand of the RNAi agent has a 2'-deoxy-modified nucleotide only at position 5 (counting from the 5' end).

In some embodiments, the antisense strand of the RNAi agent has a GNA modified nucleotide at position 7 (counting from the 5' end).In some embodiments, the RNAi agent only has 2'-OMe modifications and 2'-F modifications.

In some embodiments, an ASGPR ligand is attached to the 3'-end of the sense strand. In some embodiments, an ASGPR ligand is attached to the 5'-end of the sense strand. In some embodiments, the ASGPR ligand comprises three GalNAc derivatives attached through a trivalent branched linker.

In certain embodiments, the iRNA for use in the methods of the disclosure is an agent selected from agents listed in Tables 2-7 or 15-16. In one embodiment, the agent is AD-2217254, AD-2217251, AD-2217248, AD-2217250, AD-2217245, AD-2217252, AD-2217253, AD-2217246, AD-2217262, AD-2217258, AD-2217255, AD-2217257, or AD-2123142. These agents may further comprise a ligand.

IV. iRNAs Conjugated to Ligands

Another modification of the RNA of an iRNA of the disclosure involves chemically linking to the RNA one or more ligands, moieties or conjugates that enhance the activity, cellular distribution or cellular uptake of the iRNA. Such moieties include but are not limited to lipid moieties such as a cholesterol moiety (Letsinger *et al.*, (1989) *Proc. Natl. Acid. Sci. USA*, 86: 6553-6556), cholic acid (Manoharan *et al.*, (1994) *Biorg. Med. Chem. Let.*, 4:1053-1060), a thioether, *e.g.*, beryl-S-tritylthiol (Manoharan *et al.*, (1992) *Ann. N.Y. Acad. Sci.*, 660:306-309; Manoharan *et al.*, (1993) *Biorg. Med. Chem. Let.*, 3:2765-2770), a thiocholesterol (Oberhauser *et al.*, (1992) *Nucl. Acids Res.*, 20:533-538), an aliphatic chain, *e.g.*, dodecandiol or undecyl residues (Saison-Behmoaras *et al.*, (1991) *EMBO J*, 10:1111-1118; Kabanov *et al.*, (1990) *FEBS Lett.*, 259:327-330; Svinarchuk *et al.*, (1993) *Biochimie*, 75:49-54), a phospholipid, *e.g.*, di-hexadecyl-rac-glycerol or triethyl-ammonium 1,2-di-O-hexadecyl-rac-glycero-3-phosphonate (Manoharan *et al.*, (1995) *Tetrahedron Lett.*, 36:3651-3654; Shea *et al.*, (1990) *Nucl. Acids Res.*, 18:3777-3783), a polyamine or a polyethylene glycol chain (Manoharan *et al.*, (1995) *Nucleosides & Nucleotides*, 14:969-973), or adamantane acetic acid (Manoharan *et al.*, (1995) *Tetrahedron Lett.*, 36:3651-3654), a palmityl moiety (Mishra *et al.*, (1995) *Biochim. Biophys. Acta*, 1264:229-237), or an octadecylamine or hexylamino-carbonyloxycholesterol moiety (Crooke *et al.*, (1996) *J. Pharmacol. Exp. Ther.*, 277:923-937).

In one embodiment, a ligand alters the distribution, targeting or lifetime of an iRNA agent into which it is incorporated. In preferred embodiments a ligand provides an enhanced affinity for a selected target, *e.g.*, molecule, cell or cell type, compartment, *e.g.*, a cellular or organ compartment, tissue, organ or region of the body, as, *e.g.*, compared to a species absent such a ligand. Preferred ligands will not take part in duplex pairing in a duplexed nucleic acid.

Ligands can include a naturally occurring substance, such as a protein (*e.g.*, human serum albumin (HSA), low-density lipoprotein (LDL), or globulin); carbohydrate (*e.g.*, a dextran, pullulan, chitin, chitosan, inulin, cyclodextrin, N-acetylglucosamine, N-acetylgalactosamine or hyaluronic acid); or a lipid. The ligand can also be a recombinant or synthetic molecule, such as a synthetic polymer, *e.g.*, a synthetic polyamino acid. Examples of polyamino acids include polyamino acid is a polylysine (PLL), poly L-aspartic acid, poly L-

glutamic acid, styrene-maleic acid anhydride copolymer, poly(L-lactide-co-glycolide) copolymer, divinyl ether-maleic anhydride copolymer, N-(2-hydroxypropyl)methacrylamide copolymer (HMPA), polyethylene glycol (PEG), polyvinyl alcohol (PVA), polyurethane, poly(2-ethylacryllic acid), N-isopropylacrylamide polymers, or polyphosphazine. Example of polyamines include: polyethylenimine, polylysine (PLL), spermine, spermidine, polyamine, pseudopeptide-polyamine, peptidomimetic polyamine, dendrimer polyamine, arginine, amidine, protamine, cationic lipid, cationic porphyrin, quaternary salt of a polyamine, or an alpha helical peptide.

Ligands can also include targeting groups, *e.g.*, a cell or tissue targeting agent, *e.g.*, a lectin, glycoprotein, lipid or protein, *e.g.*, an antibody, that binds to a specified cell type. A targeting group can be a thyrotropin, melanotropin, lectin, glycoprotein, surfactant protein A, Mucin carbohydrate, multivalent lactose, multivalent galactose, N-acetyl-galactosamine, N-acetyl-glucosamine multivalent mannose, multivalent fucose, glycosylated polyaminoacids, multivalent galactose, transferrin, bisphosphonate, polyglutamate, polyaspartate, a lipid, cholesterol, a steroid, bile acid, folate, vitamin B12, vitamin A, biotin, or an RGD peptide or RGD peptide mimetic.

Ligands can be proteins, *e.g.*, glycoproteins, or peptides, *e.g.*, molecules having a specific affinity for a co-ligand, or antibodies *e.g.*, an antibody, that binds to a specified cell type such as a hepatic cell. Ligands can also include hormones and hormone receptors. They can also include non-peptidic species, such as lipids, lectins, carbohydrates, vitamins, cofactors, multivalent lactose, multivalent galactose, N-acetyl-galactosamine, N-acetyl-gulucosamine multivalent mannose, or multivalent fucose. The ligand can be, for example, a lipopolysaccharide, an activator of p38 MAP kinase, or an activator of NF-κB.

In some embodiments, a ligand attached to an iRNA as described herein acts as a pharmacokinetic modulator (PK modulator). PK modulators include lipophiles, bile acids, steroids, phospholipid analogues, peptides, protein binding agents, PEG, vitamins *etc*. Exemplary PK modulators include, but are not limited to, cholesterol, fatty acids, cholic acid, lithocholic acid, dialkylglycerides, diacylglyceride, phospholipids, sphingolipids, naproxen, ibuprofen, vitamin E, biotin *etc*. Oligonucleotides that comprise a number of phosphorothioate linkages are also known to bind to serum protein, thus short oligonucleotides, *e.g.*, oligonucleotides of about 5 bases, 10 bases, 15 bases or 20 bases, comprising multiple of phosphorothioate linkages in the backbone are also amenable to the present disclosure as ligands (*e.g.* as PK modulating ligands). In addition, aptamers that bind serum components (*e.g.* serum proteins) are also suitable for use as PK modulating ligands in the embodiments described herein.

Ligand-conjugated oligonucleotides of the disclosure may be synthesized by the use of an oligonucleotide that bears a pendant reactive functionality, such as that derived from the attachment of a linking molecule onto the oligonucleotide (described below). This reactive oligonucleotide may be reacted

directly with commercially-available ligands, ligands that are synthesized bearing any of a variety of protecting groups, or ligands that have a linking moiety attached thereto.

The oligonucleotides used in the conjugates of the present disclosure may be conveniently and routinely made through the well-known technique of solid-phase synthesis. Equipment for such synthesis is sold by several vendors including, for example, Applied Biosystems (Foster City, Calif.). Any other means for such synthesis known in the art may additionally or alternatively be employed. It is also known to use similar techniques to prepare other oligonucleotides, such as the phosphorothioates and alkylated derivatives.

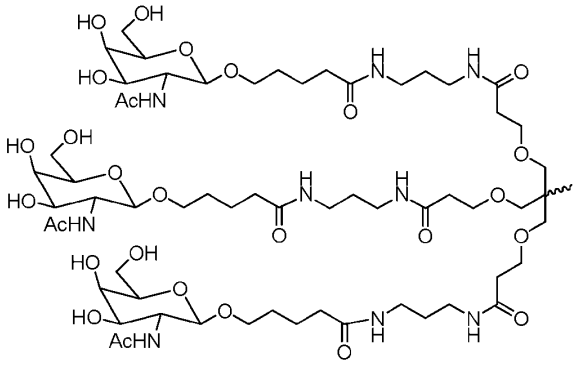
In the ligand-conjugated oligonucleotides and ligand-molecule bearing sequence-specific linked nucleosides of the present disclosure, the oligonucleotides and oligonucleosides may be assembled on a suitable DNA synthesizer utilizing standard nucleotide or nucleoside precursors, or nucleotide or nucleoside conjugate precursors that already bear the linking moiety, ligand-nucleotide or nucleoside-conjugate precursors that already bear the ligand molecule, or non-nucleoside ligand-bearing building blocks.

When using nucleotide-conjugate precursors that already bear a linking moiety, the synthesis of the sequence-specific linked nucleosides is typically completed, and the ligand molecule is then reacted with the linking moiety to form the ligand-conjugated oligonucleotide. In some embodiments, the oligonucleotides or linked nucleosides of the present disclosure are synthesized by an automated synthesizer using phosphoramidites derived from ligand-nucleoside conjugates in addition to the standard phosphoramidites and non-standard phosphoramidites that are commercially available and routinely used in oligonucleotide synthesis.

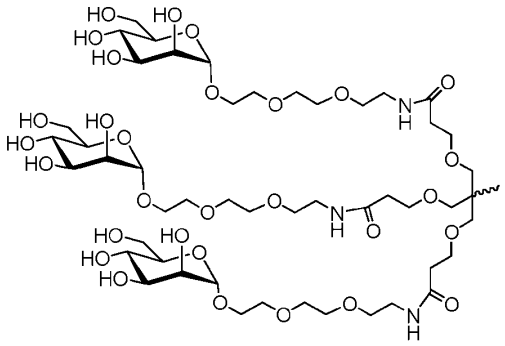
A. Carbohydrate Conjugates

In some embodiments of the compositions and methods of the disclosure, an iRNA oligonucleotide further comprises a carbohydrate. The carbohydrate conjugated iRNA are advantageous for the *in vivo* delivery of nucleic acids, as well as compositions suitable for *in vivo* therapeutic use, as described herein. As used herein, "carbohydrate" refers to a compound which is either a carbohydrate *per se* made up of one or more monosaccharide units having at least 6 carbon atoms (which can be linear, branched or cyclic) with an oxygen, nitrogen or sulfur atom bonded to each carbon atom; or a compound having as a part thereof a carbohydrate moiety made up of one or more monosaccharide units each having at least six carbon atoms (which can be linear, branched or cyclic), with an oxygen, nitrogen or sulfur atom bonded to each carbon atom. Representative carbohydrates include the sugars (mono-, di-, tri- and oligosaccharides containing from about 4, 5, 6, 7, 8, or 9 monosaccharide units), and polysaccharides such as starches, glycogen, cellulose and polysaccharide gums. Specific monosaccharides include C5 and above (*e.g.*, C5, C6, C7, or C8) sugars; di- and trisaccharides include sugars having two or three monosaccharide units (*e.g.*, C5, C6, C7, or C8).

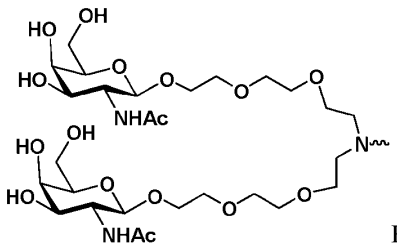
In one embodiment, a carbohydrate conjugate for use in the compositions and methods of the disclosure is selected from the group consisting of:



Formula I;



Formula II;



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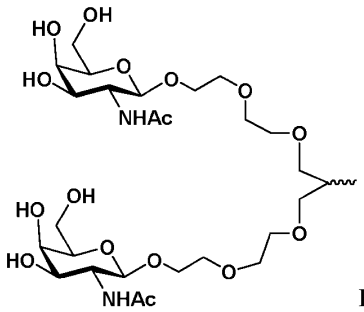

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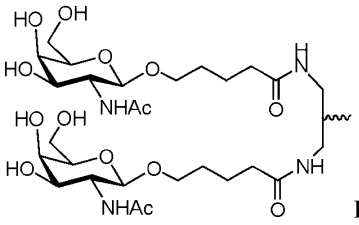

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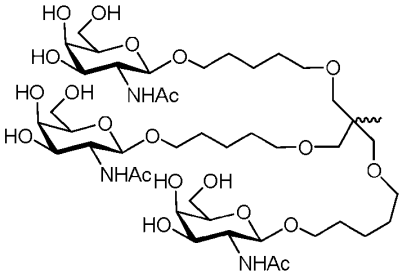

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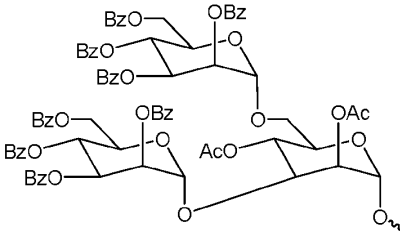

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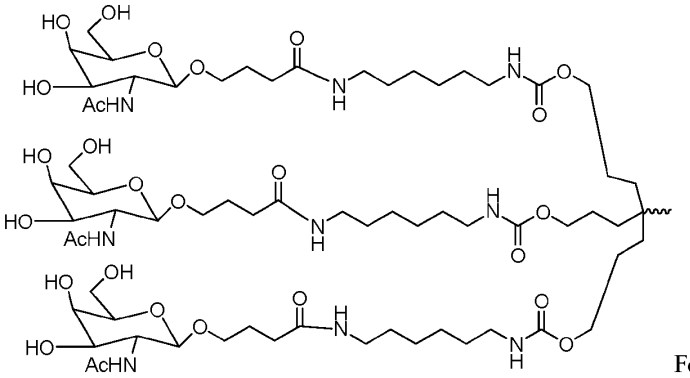

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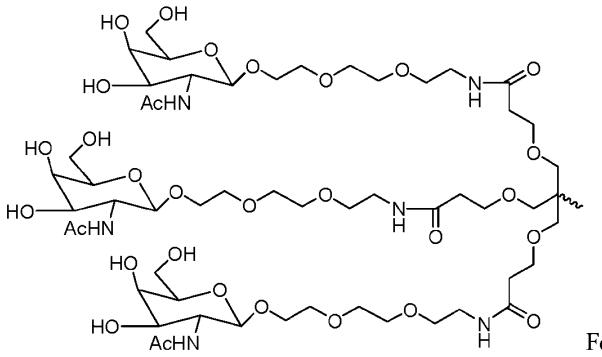

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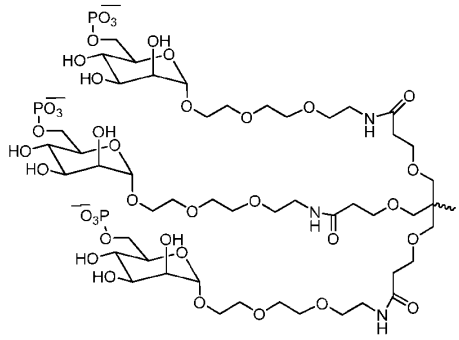

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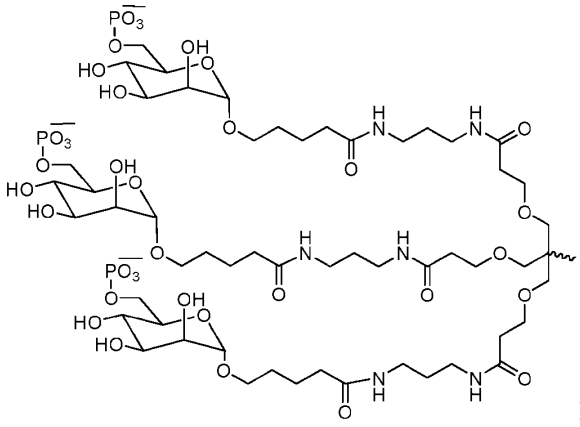

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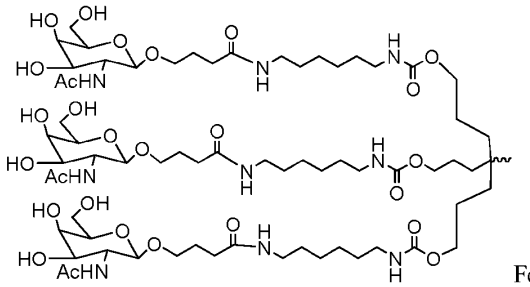

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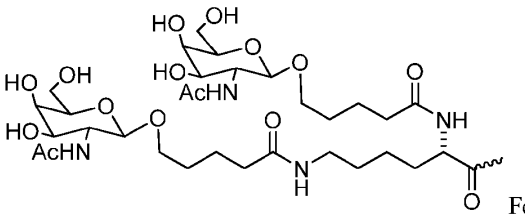
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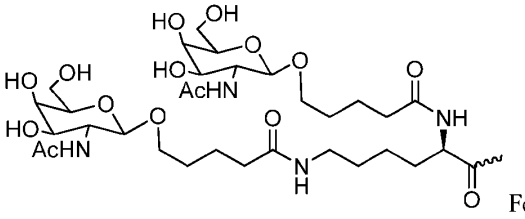
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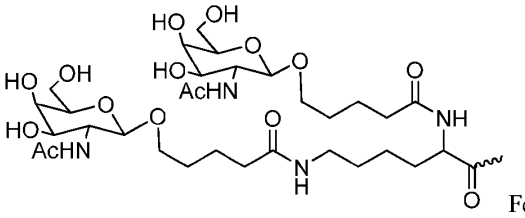
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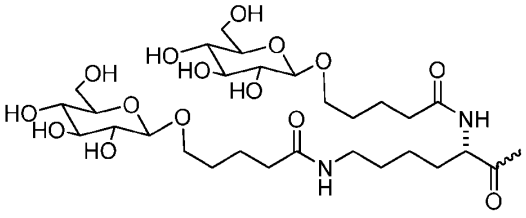
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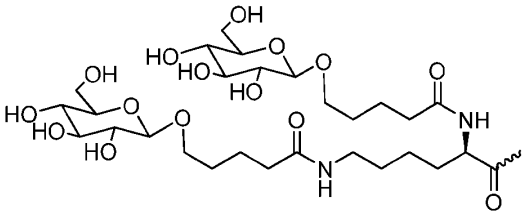
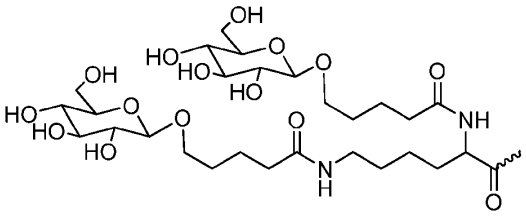
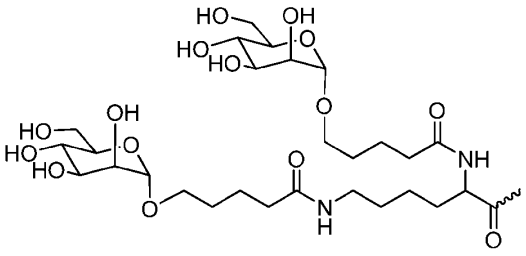

Formula XVII;


Formula XVIII;



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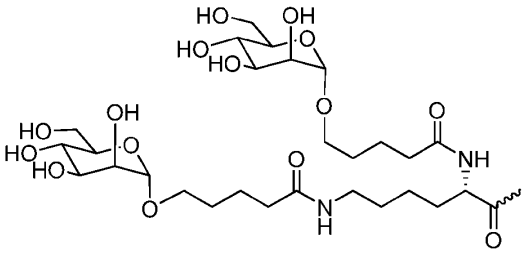
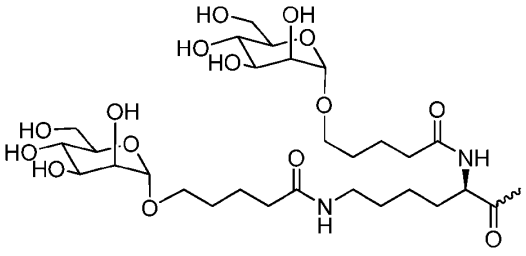
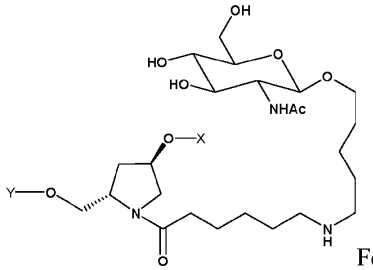


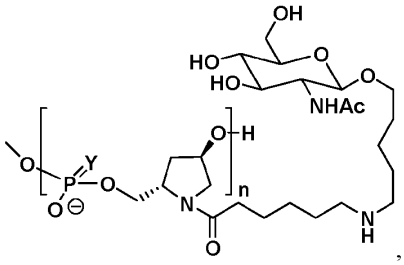
Formula XX;



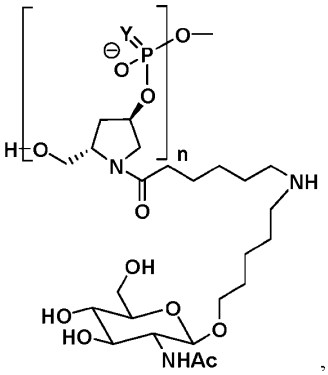
Formula XXI;



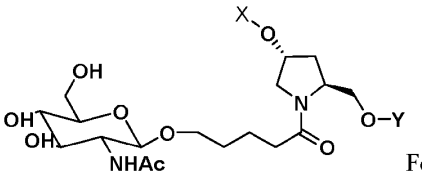
Formula XXII;



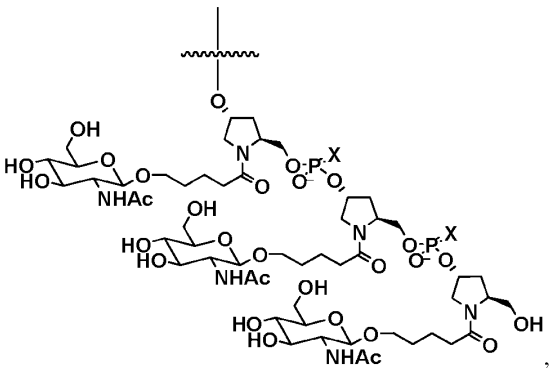
, wherein Y is O or S and n is 3 -6 (Formula XXIII);



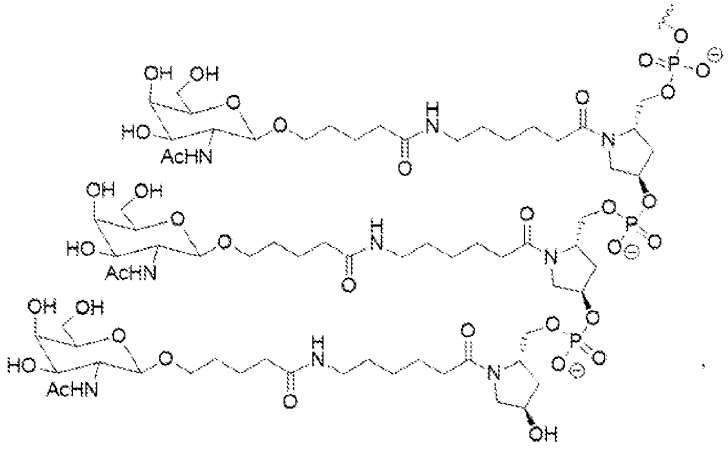
, wherein Y is O or S and n is 3-6 (Formula XXIV);



Formula XXV;



, wherein X is O or S (Formula XXVI);



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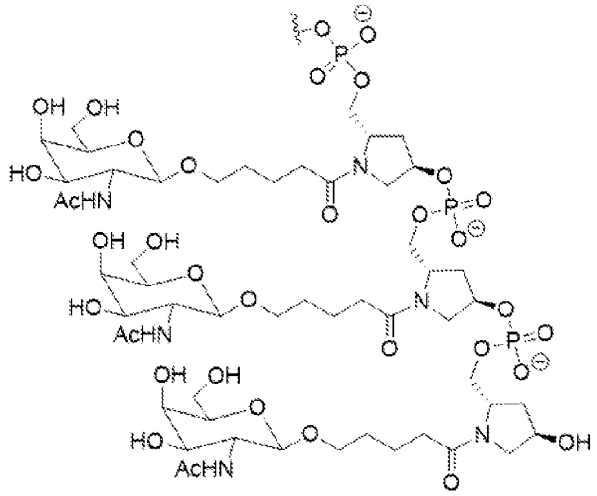
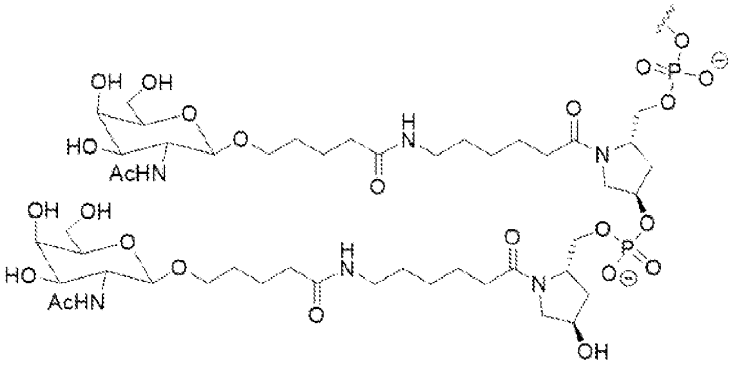
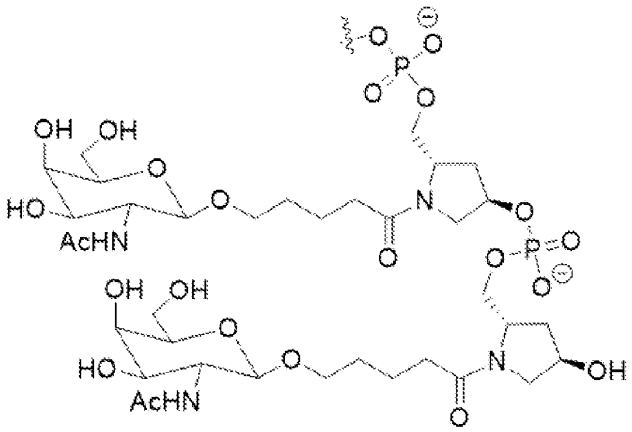


Formula XXVIII;



Formula XXIX;



Formula XXX;

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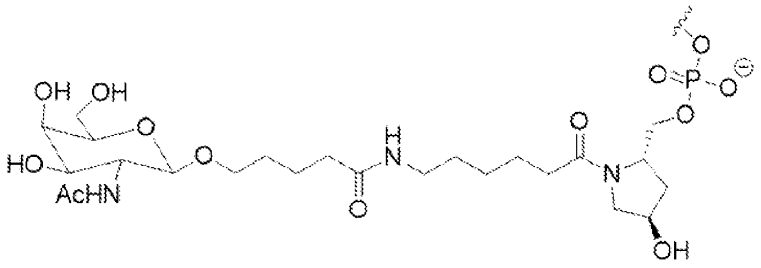
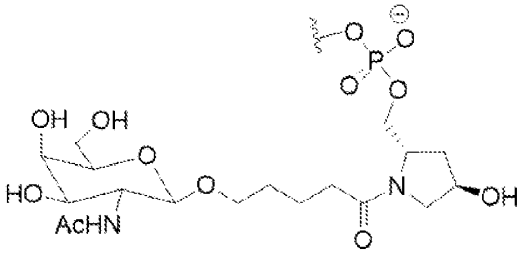
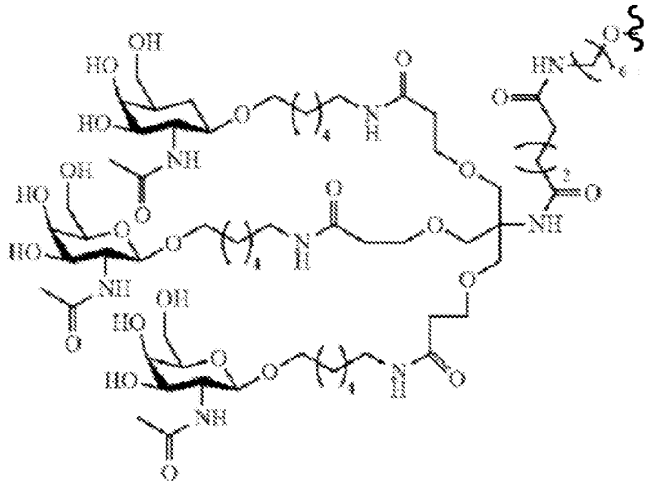


Formula XXXI;

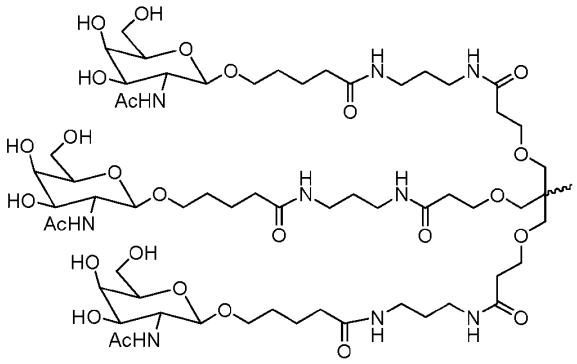


Formula XXXII; and



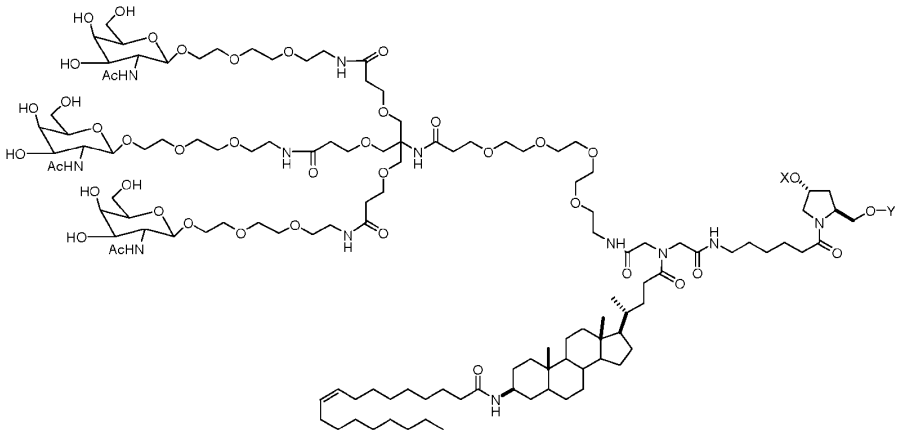
Formula XXXIII.

In another embodiment, a carbohydrate conjugate for use in the compositions and methods of the disclosure is a monosaccharide. In one embodiment, the monosaccharide is an N-acetylgalactosamine, such as



Formula I.

Another representative carbohydrate conjugate for use in the embodiments described herein includes, but is not limited to,



(Formula XXXIV),

when one of X or Y is an oligonucleotide, the other is a hydrogen.

In certain embodiments of the disclosure, the GalNAc or GalNAc derivative is attached to an iRNA agent of the disclosure *via* a monovalent linker. In some embodiments, the GalNAc or GalNAc derivative is attached to an iRNA agent of the disclosure *via* a bivalent linker. In yet other embodiments of the disclosure, the GalNAc or GalNAc derivative is attached to an iRNA agent of the disclosure *via* a trivalent linker.

In one embodiment, the double stranded RNAi agents of the disclosure comprise one GalNAc or GalNAc derivative attached to the iRNA agent, *e.g.*, the 3' or 5'end of the sense strand of a dsRNA agent as described herein. In another embodiment, the double stranded RNAi agents of the disclosure comprise a plurality (*e.g.*, 2, 3, 4, 5, or 6) of GalNAc or GalNAc derivatives, each independently attached to a plurality of nucleotides of the double stranded RNAi agent through a plurality of monovalent linkers.

In some embodiments, for example, when the two strands of an iRNA agent of the disclosure are part of one larger molecule connected by an uninterrupted chain of nucleotides between the 3'-end of one strand

and the 5'-end of the respective other strand forming a hairpin loop comprising, a plurality of unpaired nucleotides, each unpaired nucleotide within the hairpin loop may independently comprise a GalNAc or GalNAc derivative attached *via* a monovalent linker.

In some embodiments, the carbohydrate conjugate further comprises one or more additional ligands as described above, such as, but not limited to, a PK modulator and/or a cell permeation peptide.

Additional carbohydrate conjugates (and linkers) suitable for use in the present disclosure include those described in PCT Publication Nos. WO 2014/179620 and WO 2014/179627, the entire contents of each of which are incorporated herein by reference.

B. Linkers

In some embodiments, the conjugate or ligand described herein can be attached to an iRNA oligonucleotide with various linkers that can be cleavable or non-cleavable.

The term "linker" or "linking group" means an organic moiety that connects two parts of a compound, *e.g.,* covalently attaches two parts of a compound. Linkers typically comprise a direct bond or an atom such as oxygen or sulfur, a unit such as NR8, C(O), C(O)NH, SO, SO_2, SO_2NH or a chain of atoms, such as, but not limited to, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, arylalkyl, arylalkenyl, arylalkynyl, heteroarylalkyl, heteroarylalkenyl, heteroarylalkynyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, cycloalkenyl, alkylarylalkyl, alkylarylalkenyl, alkylarylalkynyl, alkenylarylalkyl, alkenylarylalkenyl, alkenylarylalkynyl, alkynylarylalkyl, alkynylarylalkenyl, alkynylarylalkynyl, alkylheteroarylalkyl, alkylheteroarylalkenyl, alkylheteroarylalkynyl, alkenylheteroarylalkyl, alkenylheteroarylalkenyl, alkenylheteroarylalkynyl, alkynylheteroarylalkyl, alkynylheteroarylalkenyl, alkynylheteroarylalkynyl, alkylheterocyclylalkyl, alkylheterocyclylalkenyl, alkylhererocyclylalkynyl, alkenylheterocyclylalkyl, alkenylheterocyclylalkenyl, alkenylheterocyclylalkynyl, alkynylheterocyclylalkyl, alkynylheterocyclylalkenyl, alkynylheterocyclylalkynyl, alkylaryl, alkenylaryl, alkynylaryl, alkylheteroaryl, alkenylheteroaryl, alkynylhereroaryl, which one or more methylenes can be interrupted or terminated by O, S, S(O), SO_2, N(R8), C(O), substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclic; where R8 is hydrogen, acyl, aliphatic or substituted aliphatic. In one embodiment, the linker is between about 1-24 atoms, 2-24, 3-24, 4-24, 5-24, 6-24, 6-18, 7-18, 8-18 atoms, 7-17, 8-17, 6-16, 7-17, or 8-16 atoms.

A cleavable linking group is one which is sufficiently stable outside the cell, but which upon entry into a target cell is cleaved to release the two parts the linker is holding together. In a preferred embodiment, the cleavable linking group is cleaved at least about 10 times, 20, times, 30 times, 40 times, 50 times, 60 times, 70 times, 80 times, 90 times or more, or at least about 100 times faster in a target cell or under a first reference condition (which can, *e.g.*, be selected to mimic or represent intracellular conditions) than in the

blood of a subject, or under a second reference condition (which can, *e.g.*, be selected to mimic or represent conditions found in the blood or serum).

Cleavable linking groups are susceptible to cleavage agents, *e.g.*, pH, redox potential or the presence of degradative molecules. Generally, cleavage agents are more prevalent or found at higher levels or activities inside cells than in serum or blood. Examples of such degradative agents include: redox agents which are selected for particular substrates or which have no substrate specificity, including, *e.g.*, oxidative or reductive enzymes or reductive agents such as mercaptans, present in cells, that can degrade a redox cleavable linking group by reduction; esterases; endosomes or agents that can create an acidic environment, *e.g.*, those that result in a pH of five or lower; enzymes that can hydrolyze or degrade an acid cleavable linking group by acting as a general acid, peptidases (which can be substrate specific), and phosphatases.

A cleavable linkage group, such as a disulfide bond can be susceptible to pH. The pH of human serum is 7.4, while the average intracellular pH is slightly lower, ranging from about 7.1-7.3. Endosomes have a more acidic pH, in the range of 5.5-6.0, and lysosomes have an even more acidic pH at around 5.0. Some linkers will have a cleavable linking group that is cleaved at a preferred pH, thereby releasing a cationic lipid from the ligand inside the cell, or into the desired compartment of the cell.

A linker can include a cleavable linking group that is cleavable by a particular enzyme. The type of cleavable linking group incorporated into a linker can depend on the cell to be targeted. For example, a liver-targeting ligand can be linked to a cationic lipid through a linker that includes an ester group. Liver cells are rich in esterases, and therefore the linker will be cleaved more efficiently in liver cells than in cell types that are not esterase-rich. Other cell-types rich in esterases include cells of the lung, renal cortex, and testis.

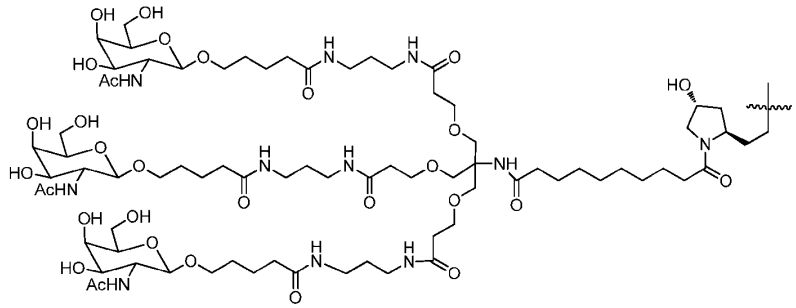
Linkers that contain peptide bonds can be used when targeting cell types rich in peptidases, such as liver cells and synoviocytes.

In general, the suitability of a candidate cleavable linking group can be evaluated by testing the ability of a degradative agent (or condition) to cleave the candidate linking group. It will also be desirable to also test the candidate cleavable linking group for the ability to resist cleavage in the blood or when in contact with other non-target tissue. Thus, one can determine the relative susceptibility to cleavage between a first and a second condition, where the first is selected to be indicative of cleavage in a target cell and the second is selected to be indicative of cleavage in other tissues or biological fluids, *e.g.*, blood or serum. The evaluations can be carried out in cell free systems, in cells, in cell culture, in organ or tissue culture, or in whole animals. It can be useful to make initial evaluations in cell-free or culture conditions and to confirm by further evaluations in whole animals. In preferred embodiments, useful candidate compounds are cleaved at least about 2, 4, 10, 20, 30, 40, 50, 60, 70, 80, 90, or about 100 times faster in the cell (or under *in vitro* conditions selected to mimic intracellular conditions) as compared to blood or serum (or under *in vitro* conditions selected to mimic extracellular conditions).

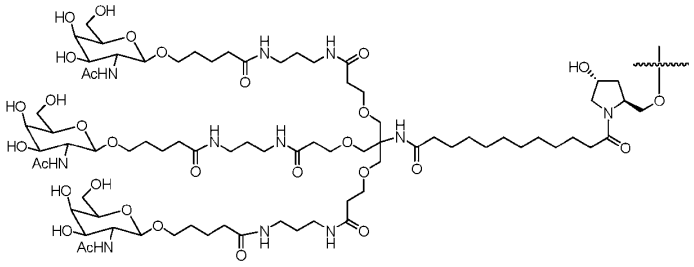
v. Peptide-based cleaving groups

In yet another embodiment, a cleavable linker comprises a peptide-based cleavable linking group. A peptide-based cleavable linking group is cleaved by enzymes such as peptidases and proteases in cells. Peptide-based cleavable linking groups are peptide bonds formed between amino acids to yield oligopeptides (*e.g.*, dipeptides, tripeptides *etc.*) and polypeptides. Peptide-based cleavable groups do not include the amide group (-C(O)NH-). The amide group can be formed between any alkylene, alkenylene or alkynelene. A peptide bond is a special type of amide bond formed between amino acids to yield peptides and proteins. The peptide based cleavage group is generally limited to the peptide bond (*i.e.*, the amide bond) formed between amino acids yielding peptides and proteins and does not include the entire amide functional group. Peptide-based cleavable linking groups have the general formula – NHCHRAC(O)NHCHRBC(O)-, where RA and RB are the R groups of the two adjacent amino acids. These candidates can be evaluated using methods analogous to those described above.

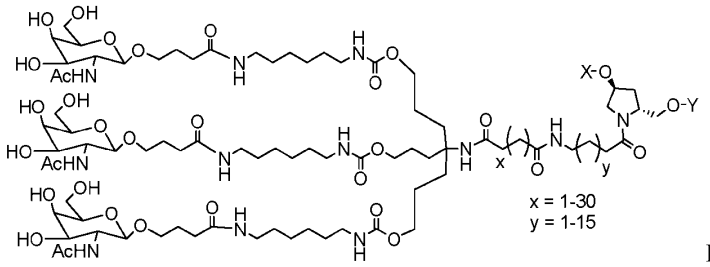
In one embodiment, an iRNA of the disclosure is conjugated to a carbohydrate through a linker. Non-limiting examples of iRNA carbohydrate conjugates with linkers of the compositions and methods of the disclosure include, but are not limited to,



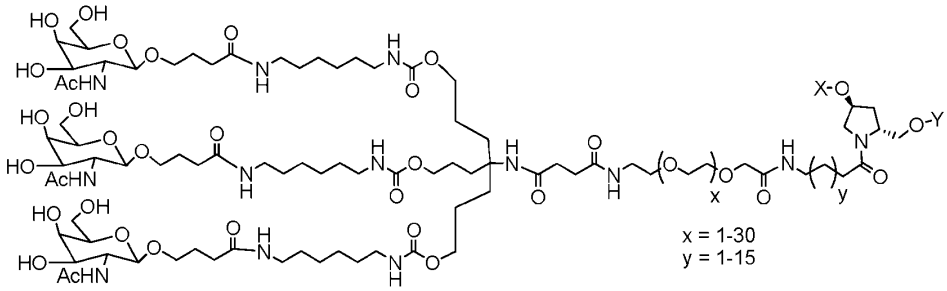
Formula XXXV;



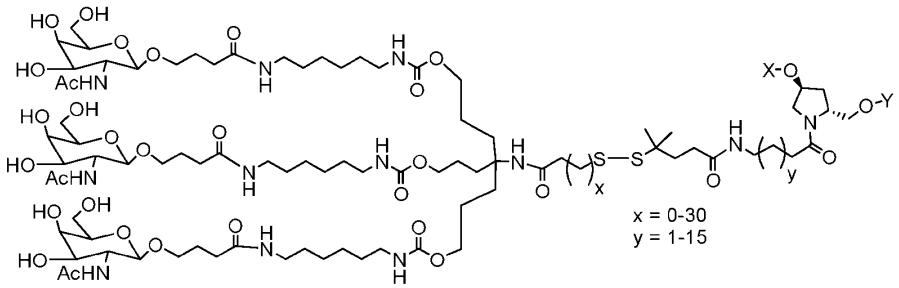
Formula XXXVI;



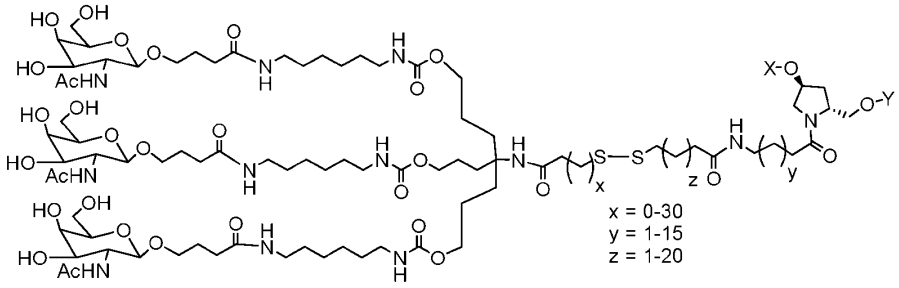
Formula XXXVII;



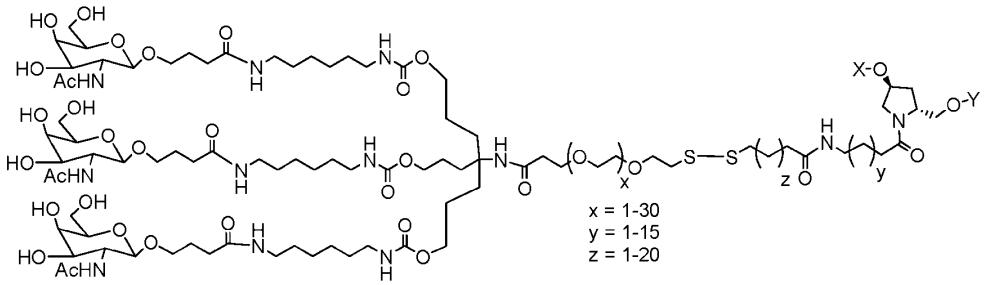
Formula XXXVIII;



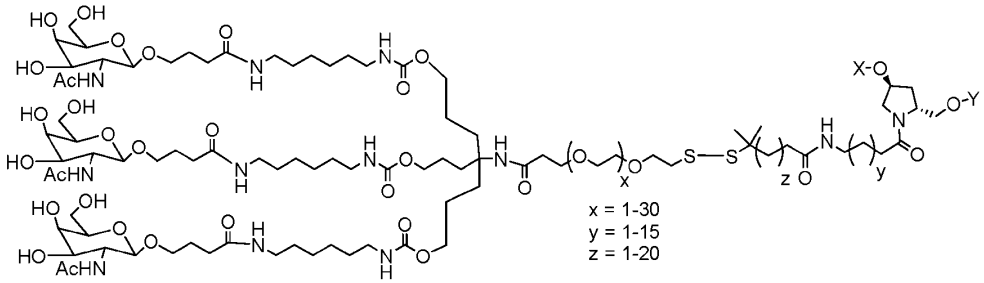
Formula XXXIX;



Formula XL;



Formula XLI; and



Formula XLII, when one of X or Y is an oligonucleotide, the other is a hydrogen.

In certain embodiments of the compositions and methods of the disclosure, a ligand is one or more GalNAc (N-acetylgalactosamine) derivatives attached through a bivalent or trivalent branched linker.

It is not necessary for all positions in a given compound to be uniformly modified, and in fact more than one of the aforementioned modifications can be incorporated in a single compound or even at a single nucleoside within an iRNA.

The present disclosure also includes iRNA compounds that are chimeric compounds.

"Chimeric" iRNA compounds or "chimeras," in the context of this disclosure, are iRNA compounds, preferably dsRNAs, which contain two or more chemically distinct regions, each made up of at least one monomer unit, *i.e.*, a nucleotide in the case of a dsRNA compound. These iRNAs typically contain at least one region wherein the RNA is modified so as to confer upon the iRNA increased resistance to nuclease degradation, increased cellular uptake, and/or increased binding affinity for the target nucleic acid. An additional region of the iRNA can serve as a substrate for enzymes capable of cleaving RNA:DNA or RNA:RNA hybrids. By way of example, RNase H is a cellular endonuclease which cleaves the RNA strand of an RNA:DNA duplex. Activation of RNase H, therefore, results in cleavage of the RNA target, thereby greatly enhancing the efficiency of iRNA inhibition of gene expression. Consequently, comparable results can often be obtained with shorter iRNAs when chimeric dsRNAs are used, compared to phosphorothioate deoxy

dsRNAs hybridizing to the same target region. Cleavage of the RNA target can be routinely detected by gel electrophoresis and, if necessary, associated nucleic acid hybridization techniques known in the art.

In certain instances, the RNA of an iRNA can be modified by a non-ligand group. A number of non-ligand molecules have been conjugated to iRNAs in order to enhance the activity, cellular distribution or cellular uptake of the iRNA, and procedures for performing such conjugations are available in the scientific literature. Such non-ligand moieties have included lipid moieties, such as cholesterol (Kubo, T. *et al.*, Biochem. Biophys. Res. Comm., 2007, 365(1):54-61; Letsinger *et al.*, Proc. Natl. Acad. Sci. USA, 1989, 86:6553), cholic acid (Manoharan *et al.*, Bioorg. Med. Chem. Lett., 1994, 4:1053), a thioether, *e.g.*, hexyl-S-tritylthiol (Manoharan *et al.*, Ann. N.Y. Acad. Sci., 1992, 660:306; Manoharan *et al.*, Bioorg. Med. Chem. Let., 1993, 3:2765), a thiocholesterol (Oberhauser *et al.*, Nucl. Acids Res., 1992, 20:533), an aliphatic chain, *e.g.*, dodecandiol or undecyl residues (Saison-Behmoaras *et al.*, EMBO J., 1991, 10:111; Kabanov *et al.*, FEBS Lett., 1990, 259:327; Svinarchuk *et al.*, Biochimie, 1993, 75:49), a phospholipid, *e.g.*, di-hexadecyl-rac-glycerol or triethylammonium 1,2-di-O-hexadecyl-rac-glycero-3-H-phosphonate (Manoharan *et al.*, Tetrahedron Lett., 1995, 36:3651; Shea *et al.*, Nucl. Acids Res., 1990, 18:3777), a polyamine or a polyethylene glycol chain (Manoharan *et al.*, Nucleosides & Nucleotides, 1995, 14:969), or adamantane acetic acid (Manoharan *et al.*, Tetrahedron Lett., 1995, 36:3651), a palmityl moiety (Mishra *et al.*, Biochim. Biophys. Acta, 1995, 1264:229), or an octadecylamine or hexylamino-carbonyl-oxycholesterol moiety (Crooke *et al.*, J. Pharmacol. Exp. Ther., 1996, 277:923). Representative United States patents that teach the preparation of such RNA conjugates have been listed above. Typical conjugation protocols involve the synthesis of an RNAs bearing an aminolinker at one or more positions of the sequence. The amino group is then reacted with the molecule being conjugated using appropriate coupling or activating reagents. The conjugation reaction can be performed either with the RNA still bound to the solid support or following cleavage of the RNA, in solution phase. Purification of the RNA conjugate by HPLC typically affords the pure conjugate.

V. Delivery of an iRNA of the Disclosure

The delivery of an iRNA of the disclosure to a cell *e.g.,* a cell within a subject, such as a human subject (*e.g.,* a subject in need thereof, such as a subject having a disorder of lipid metabolism) can be achieved in a number of different ways. For example, delivery may be performed by contacting a cell with an iRNA of the disclosure either *in vitro* or *in vivo*. *In vivo* delivery may also be performed directly by administering a composition comprising an iRNA, *e.g.,* a dsRNA, to a subject. Alternatively, *in vivo* delivery may be performed indirectly by administering one or more vectors that encode and direct the expression of the iRNA. These alternatives are discussed further below.

In general, any method of delivering a nucleic acid molecule (*in vitro* or *in vivo*) can be adapted for use with an iRNA of the disclosure (see *e.g.*, Akhtar S. and Julian RL., (1992) *Trends Cell. Biol.* 2(5):139-144 and WO94/02595, which are incorporated herein by reference in their entireties). For *in vivo* delivery, factors to consider in order to deliver an iRNA molecule include, for example, biological stability of the delivered molecule, prevention of non-specific effects, and accumulation of the delivered molecule in the target tissue. The non-specific effects of an iRNA can be minimized by local administration, for example, by direct injection or implantation into a tissue or topically administering the preparation. Local administration to a treatment site maximizes local concentration of the agent, limits the exposure of the agent to systemic tissues that can otherwise be harmed by the agent or that can degrade the agent, and permits a lower total dose of the iRNA molecule to be administered. Several studies have shown successful knockdown of gene products when an iRNA is administered locally. For example, intraocular delivery of a VEGF dsRNA by intravitreal injection in cynomolgus monkeys (Tolentino, MJ. *et al.*, (2004) *Retina* 24:132-138) and subretinal injections in mice (Reich, SJ. *et al.* (2003) *Mol. Vis.* 9:210-216) were both shown to prevent neovascularization in an experimental model of age-related macular degeneration. In addition, direct intratumoral injection of a dsRNA in mice reduces tumor volume (Pille, J. *et al.* (2005) *Mol. Ther.* 11:267-274) and can prolong survival of tumor-bearing mice (Kim, WJ. *et al.*, (2006) *Mol. Ther.* 14:343-350; Li, S. *et al.*, (2007) *Mol. Ther.* 15:515-523). For administering an iRNA systemically for the treatment of a disease, the RNA can be modified or alternatively delivered using a drug delivery system; both methods act to prevent the rapid degradation of the dsRNA by endo- and exo-nucleases in vivo. Modification of the RNA or the pharmaceutical carrier can also permit targeting of the iRNA composition to the target tissue and avoid undesirable off-target effects. iRNA molecules can be modified by chemical conjugation to lipophilic groups such as cholesterol to enhance cellular uptake and prevent degradation. For example, an iRNA directed against ApoB conjugated to a lipophilic cholesterol moiety was injected systemically into mice and resulted in knockdown of apoB mRNA in both the liver and jejunum (Soutschek, J. *et al.*, (2004) *Nature* 432:173-178). Conjugation of an iRNA to an aptamer has been shown to inhibit tumor growth and mediate tumor regression in a mouse model of prostate cancer (McNamara, JO. *et al.*, (2006) *Nat. Biotechnol.* 24:1005-1015). In an alternative embodiment, the iRNA can be delivered using drug delivery systems such as a nanoparticle, a dendrimer, a polymer, liposomes, or a cationic delivery system. Positively charged cationic delivery systems facilitate binding of an iRNA molecule (negatively charged) and also enhance interactions at the negatively charged cell membrane to permit efficient uptake of an iRNA by the cell. Cationic lipids, dendrimers, or polymers can either be bound to an iRNA, or induced to form a vesicle or micelle (see *e.g.*, Kim SH. *et al.*, (2008) *Journal of Controlled Release* 129(2):107-116) that encases an iRNA. The formation of vesicles or micelles further prevents degradation of the iRNA when administered systemically. Methods for making and administering cationic-iRNA complexes are well within the abilities of one skilled in the art (see *e.g.*, Sorensen, DR. et al. (2003) *J.*

Mol. Biol 327:761-766; Verma, UN. *et al.*, (2003) *Clin. Cancer Res.* 9:1291-1300; Arnold, AS *et al.*, (2007) *J. Hypertens.* 25:197-205, which are incorporated herein by reference in their entirety). Some non-limiting examples of drug delivery systems useful for systemic delivery of iRNAs include DOTAP (Sorensen, DR., et al (2003), supra; Verma, UN. *et al.*, (2003), supra), Oligofectamine, "solid nucleic acid lipid particles" (Zimmermann, TS. *et al.*, (2006) *Nature* 441:111-114), cardiolipin (Chien, PY. *et al.*, (2005) *Cancer Gene Ther.* 12:321-328; Pal, A. *et al.*, (2005) *Int J. Oncol.* 26:1087-1091), polyethyleneimine (Bonnet ME. *et al.*, (2008) *Pharm. Res.* Aug 16 Epub ahead of print; Aigner, A. (2006) *J. Biomed. Biotechnol.* 71659), Arg-Gly-Asp (RGD) peptides (Liu, S. (2006) *Mol. Pharm.* 3:472-487), and polyamidoamines (Tomalia, DA. *et al.*, (2007) *Biochem. Soc. Trans.* 35:61-67; Yoo, H. *et al.*, (1999) *Pharm. Res.* 16:1799-1804). In some embodiments, an iRNA forms a complex with cyclodextrin for systemic administration. Methods for administration and pharmaceutical compositions of iRNAs and cyclodextrins can be found in U.S. Patent No. 7, 427, 605, which is herein incorporated by reference in its entirety.

A. Vector encoded iRNAs of the Disclosure

iRNA targeting the GRB14 gene can be expressed from transcription units inserted into DNA or RNA vectors (see, *e.g.*, Couture, A, *et al.*, *TIG.* (1996), 12:5-10; Skillern, A., *et al.*, International PCT Publication No. WO 00/22113, Conrad, International PCT Publication No. WO 00/22114, and Conrad, U.S. Pat. No. 6,054,299). Expression can be transient (on the order of hours to weeks) or sustained (weeks to months or longer), depending upon the specific construct used and the target tissue or cell type. These transgenes can be introduced as a linear construct, a circular plasmid, or a viral vector, which can be an integrating or non-integrating vector. The transgene can also be constructed to permit it to be inherited as an extrachromosomal plasmid (Gassmann, *et al.*, (1995) *Proc. Natl. Acad. Sci. USA* 92:1292).

The individual strand or strands of an iRNA can be transcribed from a promoter on an expression vector. Where two separate strands are to be expressed to generate, for example, a dsRNA, two separate expression vectors can be co-introduced (*e.g.*, by transfection or infection) into a target cell. Alternatively, each individual strand of a dsRNA can be transcribed by promoters both of which are located on the same expression plasmid. In one embodiment, a dsRNA is expressed as inverted repeat polynucleotides joined by a linker polynucleotide sequence such that the dsRNA has a stem and loop structure.

iRNA expression vectors are generally DNA plasmids or viral vectors. Expression vectors compatible with eukaryotic cells, preferably those compatible with vertebrate cells, can be used to produce recombinant constructs for the expression of an iRNA as described herein. Eukaryotic cell expression vectors are well known in the art and are available from a number of commercial sources. Typically, such vectors are provided containing convenient restriction sites for insertion of the desired nucleic acid segment. Delivery of iRNA expressing vectors can be systemic, such as by intravenous or intramuscular administration, by administration

to target cells ex-planted from the patient followed by reintroduction into the patient, or by any other means that allows for introduction into a desired target cell.

Viral vector systems which can be utilized with the methods and compositions described herein include, but are not limited to, (a) adenovirus vectors; (b) retrovirus vectors, including but not limited to lentiviral vectors, moloney murine leukemia virus, *etc.*; (c) adeno- associated virus vectors; (d) herpes simplex virus vectors; (e) SV 40 vectors; (f) polyoma virus vectors; (g) papilloma virus vectors; (h) picornavirus vectors; (i) pox virus vectors such as an orthopox, *e.g.*, vaccinia virus vectors or avipox, *e.g.* canary pox or fowl pox; and (j) a helper-dependent or gutless adenovirus. Replication-defective viruses can also be advantageous. Different vectors will or will not become incorporated into the cells' genome. The constructs can include viral sequences for transfection, if desired. Alternatively, the construct can be incorporated into vectors capable of episomal replication, *e.g.* EPV and EBV vectors. Constructs for the recombinant expression of an iRNA will generally require regulatory elements, *e.g.*, promoters, enhancers, *etc.*, to ensure the expression of the iRNA in target cells. Other aspects to consider for vectors and constructs are known in the art.

VI. Pharmaceutical Compositions of the Disclosure

The present disclosure also includes pharmaceutical compositions and formulations which include the iRNAs of the disclosure. Accordingly, in one embodiment, provided herein are pharmaceutical compositions comprising a double stranded ribonucleic acid (dsRNA) agent that inhibits expression of growth factor receptor bound protein 14 (GRB14) in a cell, such as a liver cell, wherein the dsRNA agent comprises a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of SEQ ID NO: 1 or 3, and said antisense strand comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from the nucleotide sequence of SEQ ID NO: 2 or 4; and a pharmaceutically acceptable carrier. In some embodiments, the dsRNA agent comprises a sense strand and an antisense strand, wherein the sense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of SEQ ID NO: 1 or 3, and said antisense strand comprises at least 15 contiguous nucleotides from the nucleotide sequence of SEQ ID NO: 2 or 4.

In another embodiment, provided herein are pharmaceutical compositions comprising a dsRNA agent that inhibits expression of growth factor receptor bound protein 14 (GRB14) in a cell, such as a liver cell, wherein the dsRNA agent comprises a sense strand and an antisense strand, the antisense strand comprising a region of complementarity which comprises at least 15 contiguous nucleotides differing by no more than 1, 2, or 3 nucleotides from any one of the antisense sequences listed in Tables 2-7 or 15-16; and a pharmaceutically acceptable carrier. In some embodiments, the dsRNA agent comprises a sense strand and an antisense strand,

the antisense strand comprising a region of complementarity which comprises at least 15 contiguous nucleotides from any one of the antisense sequences listed in Tables 2-7 or 15-16.

The pharmaceutical compositions containing the iRNA of the disclosure are useful for treating a disease or disorder associated with the expression or activity of a GRB14 gene, *e.g.*, diabetes. Such pharmaceutical compositions are formulated based on the mode of delivery. One example is compositions that are formulated for systemic administration via parenteral delivery, *e.g.*, by intravenous (IV), intramuscular (IM) or for subcutaneous delivery. Another example is compositions that are formulated for direct delivery into the liver, *e.g.*, by infusion into the liver, such as by continuous pump infusion. The pharmaceutical compositions of the disclosure may be administered in dosages sufficient to inhibit expression of a GRB14 gene. In general, a suitable dose of an iRNA of the disclosure will be in the range of about 0.001 to about 200.0 milligrams per kilogram body weight of the recipient per day, generally in the range of about 1 to 50 mg per kilogram body weight per day. Typically, a suitable dose of an iRNA of the disclosure will be in the range of about 0.1 mg/kg to about 5.0 mg/kg, preferably about 0.3 mg/kg and about 3.0 mg/kg. A repeat-dose regimen may include administration of a therapeutic amount of iRNA on a regular basis, such as every other day to once a year. In certain embodiments, the iRNA is administered about once per week, once every 7-10 days, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once per month, once every 2 months, once every 3 months (once per quarter), once every 4 months, once every 5 months, or once every 6 months.

After an initial treatment regimen, the treatments can be administered on a less frequent basis.

The skilled artisan will appreciate that certain factors can influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of a composition can include a single treatment or a series of treatments. Estimates of effective dosages and *in vivo* half-lives for the individual iRNAs encompassed by the disclosure can be made using conventional methodologies or on the basis of *in vivo* testing using an appropriate animal model, as described elsewhere herein.

Advances in mouse genetics have generated a number of mouse models for the study of various human diseases, such as a GRB14-associated disease, disorder, or condition that would benefit from reduction in the expression of GRB14, including type 2 diabetes, obesity, and obesity-associated disorders. Such models can be used for in vivo testing of RNAi agents, as well as for determining a therapeutically effective dose. Suitable rodent models are known in the art and include, for example, those described in, for example, Lutz and Woods (2012) Curr. Protoc. Pharmacol. Chapter: Unit 5.61; Barrett, et al., (2016) Disease Models and

Mechanisms, 9:1245-55; and Xie et al. (2014) *PLoS ONE* 9(9): e108559 (streptozotocin-induced diabetic mice). Many experimental type 2 diabetes animal models have been established from spontaneous or experimental mutants. Such models can be used for in vivo testing of iRNA, as well as for determining a therapeutically effective dose. Additional mouse models that may be relevant to GRB14 research are known in the art and include, for example, mice and rats fed a high fat diet (HFD; also referred to as a Western diet), a methionine-choline deficient (MCD) diet, or a high-fat (15%), high-cholesterol (1%) diet (HFHC), an obese (ob/ob) mouse containing a mutation in the obese (ob) gene (Wiegman et al., (2003) Diabetes, 52:1081-1089); a mouse containing homozygous knock-out of an LDL receptor (LDLR -/- mouse; Ishibashi et al., (1993) J Clin Invest 92(2):883-893); diet-induced artherosclerosis mouse model (Ishida et al., (1991) J. Lipid. Res., 32:559-568); heterozygous lipoprotein lipase knockout mouse model (Weistock et al., (1995) J. Clin. Invest. 96(6):2555-2568); mice and rats fed a choline-deficient, L-amino acid-defined, high-fat diet (CDAHFD) (Matsumoto et al. (2013) Int. J. Exp. Path. 94:93-103); mice and rats fed a high-trans-fat, cholesterol diet (HTF-C) (Clapper et al. (2013) Am. J. Physiol. Gastrointest. Liver Physiol. 305:G483-G495); mice and rats fed a high-fat, high-cholesterol, bile salt diet (HF/HC/BS) (Matsuzawa et al. (2007) Hepatology 46:1392-1403); and mice and rats fed a high-fat diet + fructose (30%) water (Softic et al. (2018) J. Clin. Invest. 128(1)-85-96).

The pharmaceutical compositions of the present disclosure can be administered in a number of ways depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration can be topical (*e.g.*, by a transdermal patch), pulmonary, *e.g.*, by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal, oral or parenteral. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; subdermal, *e.g.*, via an implanted device; or intracranial, *e.g.*, by intraparenchymal, intrathecal or intraventricular, administration.

The iRNA can be delivered in a manner to target a particular cell or tissue, such as the liver (*e.g.*, the hepatocytes of the liver).

In some embodiments, the pharmaceutical compositions of the disclosure are suitable for intramuscular administration to a subject. In other embodiments, the pharmaceutical compositions of the disclosure are suitable for intravenous administration to a subject. In some embodiments of the disclosure, the pharmaceutical compositions of the disclosure are suitable for subcutaneous administration to a subject, *e.g.*, using a 29g or 30g needle.

The pharmaceutical compositions of the disclosure may include an RNAi agent of the disclosure in an unbuffered solution, such as saline or water, or in a buffer solution, such as a buffer solution comprising acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

In one embodiment, the pharmaceutical compositions of the disclosure, *e.g.*, such as the compositions suitable for subcutaneous administration, comprise an RNAi agent of the disclosure in phosphate buffered saline (PBS). Suitable concentrations of PBS include, for example, 1mM, 1.5 mM, 2 mM, 2.5 mM, 3 mM, 3.5 mM, 4 mM, 4.5 mM, 5 mM, 6.5 mM, 7 mM, 7.5.mM, 9 mM, 8.5 mM, 9 mM, 9.5 mM, or about 10 mM PBS. In one embodiment of the disclosure, a pharmaceutical composition of the disclosure comprises an RNAi agent of the disclosure dissolved in a solution of about 5 mM PBS (*e.g.*, 0.64 mM NaH_2PO_4, 4.36 mM Na_2HPO_4, 85 mM NaCl). Values intermediate to the above recited ranges and values are also intended to be part of this disclosure. In addition, ranges of values using a combination of any of the above recited values as upper and/or lower limits are intended to be included.

The pH of the pharmaceutical compositions of the disclosure may be between about 5.0 to about 8.0, about 5.5 to about 8.0, about 6.0 to about 8.0, about 6.5 to about 8.0, about 7.0 to about 8.0, about 5.0 to about 7.5, about 5.5 to about 7.5, about 6.0 to about 7.5, about 6.5 to about 7.5, about 5.0 to about 7.2, about 5.25 to about 7.2, about 5.5 to about 7.2, about 5.75 to about 7.2, about 6.0 to about 7.2, about 6.5 to about 7.2, or about 6.8 to about 7.2. Ranges and values intermediate to the above recited ranges and values are also intended to be part of this disclosure.

The osmolality of the pharmaceutical compositions of the disclosure may be suitable for subcutaneous administration, such as no more than about 400 mOsm/kg, *e.g.*, between 50 and 400 mOsm/kg, between 75 and 400 mOsm/kg, between 100 and 400 mOsm/kg, between 125 and 400 mOsm/kg, between 150 and 400 mOsm/kg, between 175 and 400 mOsm/kg, between 200 and 400 mOsm/kg, between 250 and 400 mOsm/kg, between 300 and 400 mOsm/kg, between 50 and 375 mOsm/kg, between 75 and 375 mOsm/kg, between 100 and 375 mOsm/kg, between 125 and 375 mOsm/kg, between 150 and 375 mOsm/kg, between 175 and 375 mOsm/kg, between 200 and 375 mOsm/kg, between 250 and 375 mOsm/kg, between 300 and 375 mOsm/kg, between 50 and 350 mOsm/kg, between 75 and 350 mOsm/kg, between 100 and 350 mOsm/kg, between 125 and 350 mOsm/kg, between 150 and 350 mOsm/kg, between 175 and 350 mOsm/kg, between 200 and 350 mOsm/kg, between 250 and 350 mOsm/kg, between 50 and 325 mOsm/kg, between 75 and 325 mOsm/kg, between 100 and 325 mOsm/kg, between 125 and 325 mOsm/kg, between 150 and 325 mOsm/kg, between 175 and 325 mOsm/kg, between 200 and 325 mOsm/kg, between 250 and 325 mOsm/kg, between 300 and 325 mOsm/kg, between 300 and 350 mOsm/kg, between 50 and 300 mOsm/kg, between 75 and 300 mOsm/kg, between 100 and 300 mOsm/kg, between 125 and 300 mOsm/kg, between 150 and 300 mOsm/kg, between 175 and 300 mOsm/kg, between 200 and 300 mOsm/kg, between 250 and 300, between 50 and 250 mOsm/kg, between 75 and 250 mOsm/kg, between 100 and 250 mOsm/kg, between 125 and 250 mOsm/kg, between 150 and 250 mOsm/kg, between 175 and 350 mOsm/kg, between 200 and 250 mOsm/kg, *e.g.*, about 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 120, 125, 130, 135, 140, 145, 150, 155, 160, 165, 170, 175, 180, 185, 190, 195, 200, 205, 210, 215, 220, 225, 230, 235, 240, 245, 250, 255, 260, 265, 270, 275, 280, 285, 295, 300, 305, 310, 320, 325, 330, 335, 340,

345, 350, 355, 360, 365, 370, 375, 380, 385, 390, 395, or about 400 mOsm/kg. Ranges and values intermediate to the above recited ranges and values are also intended to be part of this disclosure.

The pharmaceutical compositions of the disclosure comprising the RNAi agents of the disclosure, may be present in a vial that contains about 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, or about 2.0 mL of the pharmaceutical composition. The concentration of the RNAi agents in the pharmaceutical compositions of the disclosure may be about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 105, 110, 115, 130, 125, 130, 135, 140, 145, 150, 175, 180, 185, 190, 195, 200, 205, 210, 215, 230, 225, 230, 235, 240, 245, 250, 275, 280, 285, 290, 295, 300, 305, 310, 315, 330, 325, 330, 335, 340, 345, 350, 375, 380, 385, 390, 395, 400, 405, 410, 415, 430, 425, 430, 435, 440, 445, 450, 475, 480, 485, 490, 495, or about 500 mg/mL. In one embodiment, the concentration of the RNAi agents in the pharmaceutical compositions of the disclosure is about 100 mg/mL. Values intermediate to the above recited ranges and values are also intended to be part of this disclosure.

The pharmaceutical compositions of the disclosure may comprise a dsRNA agent of the disclosure in a free acid form. In other embodiments of the disclosure, the pharmaceutical compositions of the disclosure may comprise a dsRNA agent of the disclosure in a salt form, such as a sodium salt form. In certain embodiments, when the dsRNA agents of the disclosure are in the sodium salt form, sodium ions are present in the agent as counterions for substantially all of the phosphodiester and/or phosphorothioate groups present in the agent. Agents in which substantially all of the phosphodiester and/or phosphorothioate linkages have a sodium counterion include not more than 5, 4, 3, 2, or 1 phosphodiester and/or phosphorothioate linkages without a sodium counterion. In some embodiments, when the dsRNA agents of the disclosure are in the sodium salt form, sodium ions are present in the agent as counterions for all of the phosphodiester and/or phosphorothioate groups present in the agent.

Compositions and formulations for oral administration include powders or granules, microparticulates, nanoparticulates, suspensions or solutions in water or non-aqueous media, capsules, gel capsules, sachets, tablets or minitablets. Thickeners, flavoring agents, diluents, emulsifiers, dispersing aids or binders can be desirable. In some embodiments, oral formulations are those in which dsRNAs featured in the disclosure are administered in conjunction with one or more penetration enhancer surfactants and chelators. Suitable surfactants include fatty acids and/or esters or salts thereof, bile acids and/or salts thereof. Suitable bile acids/salts include chenodeoxycholic acid (CDCA) and ursodeoxychenodeoxycholic acid (UDCA), cholic acid, dehydrocholic acid, deoxycholic acid, glucholic acid, glycholic acid, glycodeoxycholic acid, taurocholic acid, taurodeoxycholic acid, sodium tauro-24,25-dihydro-fusidate and sodium glycodihydrofusidate. Suitable fatty acids include arachidonic acid, undecanoic acid, oleic acid, lauric acid, caprylic acid, capric acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein, dilaurin, glyceryl 1-monocaprate, 1-dodecylazacycloheptan-2-one, an acylcarnitine, an acylcholine, or a monoglyceride, a diglyceride or a pharmaceutically acceptable salt thereof (*e.g.*, sodium). In some

embodiments, combinations of penetration enhancers are used, for example, fatty acids/salts in combination with bile acids/salts. One exemplary combination is the sodium salt of lauric acid, capric acid and UDCA. Further penetration enhancers include polyoxyethylene-9-lauryl ether, polyoxyethylene-20-cetyl ether. DsRNAs featured in the disclosure can be delivered orally, in granular form including sprayed dried particles, or complexed to form micro or nanoparticles. DsRNA complexing agents include poly-amino acids; polyimines; polyacrylates; polyalkylacrylates, polyoxethanes, polyalkylcyanoacrylates; cationized gelatins, albumins, starches, acrylates, polyethyleneglycols (PEG) and starches; polyalkylcyanoacrylates; DEAE-derivatized polyimines, pollulans, celluloses and starches. Suitable complexing agents include chitosan, N-trimethylchitosan, poly-L-lysine, polyhistidine, polyornithine, polyspermines, protamine, polyvinylpyridine, polythiodiethylaminomethylethylene P(TDAE), polyaminostyrene (*e.g.,* p-amino), poly(methylcyanoacrylate), poly(ethylcyanoacrylate), poly(butylcyanoacrylate), poly(isobutylcyanoacrylate), poly(isohexylcynaoacrylate), DEAE-methacrylate, DEAE-hexylacrylate, DEAE-acrylamide, DEAE-albumin and DEAE-dextran, polymethylacrylate, polyhexylacrylate, poly(D,L-lactic acid), poly(DL-lactic-co-glycolic acid (PLGA), alginate, and polyethyleneglycol (PEG). Oral formulations for dsRNAs and their preparation are described in detail in U.S. Patent 6,887,906, US Publication. No. 20030027780, and U.S. Patent No. 6,747,014, each of which is incorporated herein by reference.

Compositions and formulations for parenteral, intraparenchymal (into the brain), intrathecal, intraventricular or intrahepatic administration can include sterile aqueous solutions which can also contain buffers, diluents and other suitable additives such as, but not limited to, penetration enhancers, carrier compounds and other pharmaceutically acceptable carriers or excipients.

Pharmaceutical compositions of the present disclosure include, but are not limited to, solutions, emulsions, and liposome-containing formulations. These compositions can be generated from a variety of components that include, but are not limited to, preformed liquids, self-emulsifying solids and self-emulsifying semisolids. Particularly preferred are formulations that target the liver when treating hepatic disorders such as hepatic carcinoma.

The pharmaceutical formulations of the present disclosure, which can conveniently be presented in unit dosage form, can be prepared according to conventional techniques well known in the pharmaceutical industry. Such techniques include the step of bringing into association the active ingredients with the pharmaceutical carrier(s) or excipient(s). In general, the formulations are prepared by uniformly and intimately bringing into association the active ingredients with liquid carriers or finely divided solid carriers or both, and then, if necessary, shaping the product.

The compositions of the present disclosure can be formulated into any of many possible dosage forms such as, but not limited to, tablets, capsules, gel capsules, liquid syrups, soft gels, suppositories, and enemas. The compositions of the present disclosure can also be formulated as suspensions in aqueous, non-aqueous or

mixed media. Aqueous suspensions can further contain substances which increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol and/or dextran. The suspension can also contain stabilizers.

Many liposomes comprising lipids derivatized with one or more hydrophilic polymers, and methods of preparation thereof, are known in the art. Sunamoto *et al.* (Bull. *Chem. Soc. Jpn.*, 1980, 53, 2778) described liposomes comprising a nonionic detergent, $2C_{1215G}$, that contains a PEG moiety. Illum *et al.* (*FEBS Lett.*, 1984, 167, 79) noted that hydrophilic coating of polystyrene particles with polymeric glycols results in significantly enhanced blood half-lives. Synthetic phospholipids modified by the attachment of carboxylic groups of polyalkylene glycols (*e.g.*, PEG) are described by Sears (U.S. Pat. Nos. 4,426,330 and 4,534,899). Klibanov *et al.* (*FEBS Lett.*, 1990, 268, 235) described experiments demonstrating that liposomes comprising phosphatidylethanolamine (PE) derivatized with PEG or PEG stearate have significant increases in blood circulation half-lives. Blume *et al.* (*Biochimica et Biophysica Acta*, 1990, 1029, 91) extended such observations to other PEG-derivatized phospholipids, *e.g.*, DSPE-PEG, formed from the combination of distearoylphosphatidylethanolamine (DSPE) and PEG. Liposomes having covalently bound PEG moieties on their external surface are described in European Patent No. EP 0 445 131 B1 and WO 90/04384 to Fisher. Liposome compositions containing 1-20 mole percent of PE derivatized with PEG, and methods of use thereof, are described by Woodle *et al.* (U.S. Pat. Nos. 5,013,556 and 5,356,633) and Martin *et al.* (U.S. Pat. No. 5,213,804 and European Patent No. EP 0 496 813 B1). Liposomes comprising a number of other lipid-polymer conjugates are disclosed in WO 91/05545 and U.S. Pat. No. 5,225,212 (both to Martin *et al.*) and in WO 94/20073 (Zalipsky *et al.*). Liposomes comprising PEG-modified ceramide lipids are described in WO 96/10391 (Choi *et al*). U.S. Pat. No. 5,540,935 (Miyazaki *et al.*) and U.S. Pat. No. 5,556,948 (Tagawa *et al.*) describe PEG-containing liposomes that can be further derivatized with functional moieties on their surfaces.

A. Additional Formulations

i. Emulsions

The compositions of the present disclosure can be prepared and formulated as emulsions. Emulsions are typically heterogeneous systems of one liquid dispersed in another in the form of droplets usually exceeding 0.1μm in diameter (see *e.g.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Allen, LV., Popovich NG., and Ansel HC., 2004, Lippincott Williams & Wilkins (8th ed.), New York, NY; Idson, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199; Rosoff, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., Volume 1, p. 245; Block in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 2, p. 335; Higuchi *et al.*, in Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa., 1985, p. 301).

Emulsions are often biphasic systems comprising two immiscible liquid phases intimately mixed and dispersed with each other. In general, emulsions can be of either the water-in-oil (w/o) or the oil-in-water (o/w) variety. When an aqueous phase is finely divided into and dispersed as minute droplets into a bulk oily phase, the resulting composition is called a water-in-oil (w/o) emulsion. Alternatively, when an oily phase is finely divided into and dispersed as minute droplets into a bulk aqueous phase, the resulting composition is called an oil-in-water (o/w) emulsion. Emulsions can contain additional components in addition to the dispersed phases, and the active drug which can be present as a solution in either aqueous phase, oily phase or itself as a separate phase. Pharmaceutical excipients such as emulsifiers, stabilizers, dyes, and anti-oxidants can also be present in emulsions as needed. Pharmaceutical emulsions can also be multiple emulsions that are comprised of more than two phases such as, for example, in the case of oil-in-water-in-oil (o/w/o) and water-in-oil-in-water (w/o/w) emulsions. Such complex formulations often provide certain advantages that simple binary emulsions do not. Multiple emulsions in which individual oil droplets of an o/w emulsion enclose small water droplets constitute a w/o/w emulsion. Likewise, a system of oil droplets enclosed in globules of water stabilized in an oily continuous phase provides an o/w/o emulsion.

Emulsions are characterized by little or no thermodynamic stability. Often, the dispersed or discontinuous phase of the emulsion is well dispersed into the external or continuous phase and maintained in this form through the means of emulsifiers or the viscosity of the formulation. Either of the phases of the emulsion can be a semisolid or a solid, as is the case of emulsion-style ointment bases and creams. Other means of stabilizing emulsions entail the use of emulsifiers that can be incorporated into either phase of the emulsion. Emulsifiers can broadly be classified into four categories: synthetic surfactants, naturally occurring emulsifiers, absorption bases, and finely dispersed solids (see *e.g.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Allen, LV., Popovich NG., and Ansel HC., 2004, Lippincott Williams & Wilkins (8th ed.), New York, NY; Idson, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

Synthetic surfactants, also known as surface active agents, have found wide applicability in the formulation of emulsions and have been reviewed in the literature (see *e.g.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Allen, LV., Popovich NG., and Ansel HC., 2004, Lippincott Williams & Wilkins (8th ed.), New York, NY; Rieger, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285; Idson, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), Marcel Dekker, Inc., New York, N.Y., 1988, volume 1, p. 199). Surfactants are typically amphiphilic and comprise a hydrophilic and a hydrophobic portion. The ratio of the hydrophilic to the hydrophobic nature of the surfactant has been termed the hydrophile/lipophile balance (HLB) and is a valuable tool in categorizing and selecting surfactants in the preparation of formulations. Surfactants can be classified into different classes based on the nature of the hydrophilic group: nonionic,

anionic, cationic and amphoteric (see *e.g.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Allen, LV., Popovich NG., and Ansel HC., 2004, Lippincott Williams & Wilkins (8th ed.), New York, NY Rieger, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 285).

Naturally occurring emulsifiers used in emulsion formulations include lanolin, beeswax, phosphatides, lecithin and acacia. Absorption bases possess hydrophilic properties such that they can soak up water to form w/o emulsions yet retain their semisolid consistencies, such as anhydrous lanolin and hydrophilic petrolatum. Finely divided solids have also been used as good emulsifiers especially in combination with surfactants and in viscous preparations. These include polar inorganic solids, such as heavy metal hydroxides, nonswelling clays such as bentonite, attapulgite, hectorite, kaolin, montmorillonite, colloidal aluminum silicate and colloidal magnesium aluminum silicate, pigments and nonpolar solids such as carbon or glyceryl tristearate.

A large variety of non-emulsifying materials are also included in emulsion formulations and contribute to the properties of emulsions. These include fats, oils, waxes, fatty acids, fatty alcohols, fatty esters, humectants, hydrophilic colloids, preservatives and antioxidants (Block, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 335; Idson, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 199).

Hydrophilic colloids or hydrocolloids include naturally occurring gums and synthetic polymers such as polysaccharides (for example, acacia, agar, alginic acid, carrageenan, guar gum, karaya gum, and tragacanth), cellulose derivatives (for example, carboxymethylcellulose and carboxypropylcellulose), and synthetic polymers (for example, carbomers, cellulose ethers, and carboxyvinyl polymers). These disperse or swell in water to form colloidal solutions that stabilize emulsions by forming strong interfacial films around the dispersed-phase droplets and by increasing the viscosity of the external phase.

Since emulsions often contain a number of ingredients such as carbohydrates, proteins, sterols and phosphatides that can readily support the growth of microbes, these formulations often incorporate preservatives. Commonly used preservatives included in emulsion formulations include methyl paraben, propyl paraben, quaternary ammonium salts, benzalkonium chloride, esters of p-hydroxybenzoic acid, and boric acid. Antioxidants are also commonly added to emulsion formulations to prevent deterioration of the formulation. Antioxidants used can be free radical scavengers such as tocopherols, alkyl gallates, butylated hydroxyanisole, butylated hydroxytoluene, or reducing agents such as ascorbic acid and sodium metabisulfite, and antioxidant synergists such as citric acid, tartaric acid, and lecithin.

ii. *Microemulsions*

In one embodiment of the present disclosure, the compositions of iRNAs and nucleic acids are formulated as microemulsions. A microemulsion can be a system of water, oil and amphiphile which is a

single optically isotropic and thermodynamically stable liquid solution (see *e.g.*, Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems, Allen, LV., Popovich NG., and Ansel HC., 2004, Lippincott Williams & Wilkins (8th ed.), New York, NY; Rosoff, in Pharmaceutical Dosage Forms, Lieberman, Rieger and Banker (Eds.), 1988, Marcel Dekker, Inc., New York, N.Y., volume 1, p. 245). Typically, microemulsions are systems that are prepared by first dispersing an oil in an aqueous surfactant solution and then adding a sufficient amount of a fourth component, generally an intermediate chain-length alcohol to form a transparent system. Therefore, microemulsions have also been described as thermodynamically stable, isotropically clear dispersions of two immiscible liquids that are stabilized by interfacial films of surface-active molecules (Leung and Shah, in: Controlled Release of Drugs: Polymers and Aggregate Systems, Rosoff, M., Ed., 1989, VCH Publishers, New York, pages 185-215). Microemulsions commonly are prepared via a combination of three to five components that include oil, water, surfactant, cosurfactant and electrolyte. Whether the microemulsion is of the water-in-oil (w/o) or an oil-in-water (o/w) type is dependent on the properties of the oil and surfactant used and on the structure and geometric packing of the polar heads and hydrocarbon tails of the surfactant molecules (Schott, in Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa., 1985, p. 271).

Surfactants used in the preparation of microemulsions include, but are not limited to, ionic surfactants, non-ionic surfactants, Brij 96, polyoxyethylene oleyl ethers, polyglycerol fatty acid esters, tetraglycerol monolaurate (ML310), tetraglycerol monooleate (MO310), hexaglycerol monooleate (PO310), hexaglycerol pentaoleate (PO500), decaglycerol monocaprate (MCA750), decaglycerol monooleate (MO750), decaglycerol sequioleate (SO750), decaglycerol decaoleate (DAO750), alone or in combination with cosurfactants. The cosurfactant, usually a short-chain alcohol such as ethanol, 1-propanol, and 1-butanol, serves to increase the interfacial fluidity by penetrating into the surfactant film and consequently creating a disordered film because of the void space generated among surfactant molecules. Microemulsions can, however, be prepared without the use of cosurfactants and alcohol-free self-emulsifying microemulsion systems are known in the art. The aqueous phase can typically be, but is not limited to, water, an aqueous solution of the drug, glycerol, PEG300, PEG400, polyglycerols, propylene glycols, and derivatives of ethylene glycol. The oil phase can include, but is not limited to, materials such as Captex 300, Captex 355, Capmul MCM, fatty acid esters, medium chain (C8-C12) mono, di, and tri-glycerides, polyoxyethylated glyceryl fatty acid esters, fatty alcohols, polyglycolized glycerides, saturated polyglycolized C8-C10 glycerides, vegetable oils and silicone oil.

Microemulsions are particularly of interest from the standpoint of drug solubilization and the enhanced absorption of drugs. Lipid based microemulsions (both o/w and w/o) have been proposed to enhance the oral bioavailability of drugs, including peptides (see *e.g.*, U.S. Patent Nos. 6,191,105; 7,063,860; 7,070,802; 7,157,099; Constantinides *et al.*, Pharmaceutical Research, 1994, 11, 1385-1390; Ritschel, Meth.

Find. Exp. Clin. Pharmacol., 1993, 13, 205). Microemulsions afford advantages of improved drug solubilization, protection of drug from enzymatic hydrolysis, possible enhancement of drug absorption due to surfactant-induced alterations in membrane fluidity and permeability, ease of preparation, ease of oral administration over solid dosage forms, improved clinical potency, and decreased toxicity (see *e.g.*, U.S. Patent Nos. 6,191,105; 7,063,860; 7,070,802; 7,157,099; Constantinides *et al.*, Pharmaceutical Research, 1994, 11, 1385; Ho *et al.*, J. Pharm. Sci., 1996, 85, 138-143). Often microemulsions can form spontaneously when their components are brought together at ambient temperature. This can be particularly advantageous when formulating thermolabile drugs, peptides or iRNAs. Microemulsions have also been effective in the transdermal delivery of active components in both cosmetic and pharmaceutical applications. It is expected that the microemulsion compositions and formulations of the present disclosure will facilitate the increased systemic absorption of iRNAs and nucleic acids from the gastrointestinal tract, as well as improve the local cellular uptake of iRNAs and nucleic acids.

Microemulsions of the present disclosure can also contain additional components and additives such as sorbitan monostearate (Grill 3), Labrasol, and penetration enhancers to improve the properties of the formulation and to enhance the absorption of the iRNAs and nucleic acids of the present disclosure. Penetration enhancers used in the microemulsions of the present disclosure can be classified as belonging to one of five broad categories--surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactants (Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, p. 92). Each of these classes has been discussed above.

iii. *Microparticles*

An RNAi agent of the disclosure may be incorporated into a particle, *e.g.*, a microparticle. Microparticles can be produced by spray-drying, but may also be produced by other methods including lyophilization, evaporation, fluid bed drying, vacuum drying, or a combination of these techniques.

iv. *Penetration Enhancers*

In one embodiment, the present disclosure employs various penetration enhancers to effect the efficient delivery of nucleic acids, particularly iRNAs, to the skin of animals. Most drugs are present in solution in both ionized and nonionized forms. However, usually only lipid soluble or lipophilic drugs readily cross cell membranes. It has been discovered that even non-lipophilic drugs can cross cell membranes if the membrane to be crossed is treated with a penetration enhancer. In addition to aiding the diffusion of non-lipophilic drugs across cell membranes, penetration enhancers also enhance the permeability of lipophilic drugs.

Penetration enhancers can be classified as belonging to one of five broad categories, *i.e.*, surfactants, fatty acids, bile salts, chelating agents, and non-chelating non-surfactants (see *e.g.*, Malmsten, M. Surfactants and polymers in drug delivery, Informa Health Care, New York, NY, 2002; Lee *et al.*, Critical Reviews in

Therapeutic Drug Carrier Systems, 1991, p.92). Each of the above mentioned classes of penetration enhancers are described below in greater detail.

Surfactants (or "surface-active agents") are chemical entities which, when dissolved in an aqueous solution, reduce the surface tension of the solution or the interfacial tension between the aqueous solution and another liquid, with the result that absorption of iRNAs through the mucosa is enhanced. In addition to bile salts and fatty acids, these penetration enhancers include, for example, sodium lauryl sulfate, polyoxyethylene-9-lauryl ether and polyoxyethylene-20-cetyl ether) (see *e.g.*, Malmsten, M. Surfactants and polymers in drug delivery, Informa Health Care, New York, NY, 2002; Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, p.92); and perfluorochemical emulsions, such as FC-43. Takahashi *et al.*, J. Pharm. Pharmacol., 1988, 40, 252).

Various fatty acids and their derivatives which act as penetration enhancers include, for example, oleic acid, lauric acid, capric acid (n-decanoic acid), myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein (1-monooleoyl-rac-glycerol), dilaurin, caprylic acid, arachidonic acid, glycerol 1-monocaprate, 1-dodecylazacycloheptan-2-one, acylcarnitines, acylcholines, C_{1-20} alkyl esters thereof (*e.g.*, methyl, isopropyl and t-butyl), and mono- and di-glycerides thereof (*i.e.*, oleate, laurate, caprate, myristate, palmitate, stearate, linoleate, *etc.*) (see *e.g.*, Touitou, E. et al. Enhancement in Drug Delivery, CRC Press, Danvers, MA, 2006; Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, p.92; Muranishi, Critical Reviews in Therapeutic Drug Carrier Systems, 1990, 7, 1-33; El Hariri *et al.*, J. Pharm. Pharmacol., 1992, 44, 651-654).

The physiological role of bile includes the facilitation of dispersion and absorption of lipids and fat-soluble vitamins (see *e.g.*, Malmsten, M. Surfactants and polymers in drug delivery, Informa Health Care, New York, NY, 2002; Brunton, Chapter 38 in: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 9th Ed., Hardman *et al.* Eds., McGraw-Hill, New York, 1996, pp. 934-935). Various natural bile salts, and their synthetic derivatives, act as penetration enhancers. Thus the term "bile salts" includes any of the naturally occurring components of bile as well as any of their synthetic derivatives. Suitable bile salts include, for example, cholic acid (or its pharmaceutically acceptable sodium salt, sodium cholate), dehydrocholic acid (sodium dehydrocholate), deoxycholic acid (sodium deoxycholate), glucholic acid (sodium glucholate), glycholic acid (sodium glycocholate), glycodeoxycholic acid (sodium glycodeoxycholate), taurocholic acid (sodium taurocholate), taurodeoxycholic acid (sodium taurodeoxycholate), chenodeoxycholic acid (sodium chenodeoxycholate), ursodeoxycholic acid (UDCA), sodium tauro-24,25-dihydro-fusidate (STDHF), sodium glycodihydrofusidate and polyoxyethylene-9-lauryl ether (POE) (see *e.g.*, Malmsten, M. Surfactants and polymers in drug delivery, Informa Health Care, New York, NY, 2002; Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, page 92; Swinyard, Chapter 39 In: Remington's Pharmaceutical Sciences, 18th Ed., Gennaro, ed., Mack Publishing Co., Easton, Pa., 1990, pages 782-783;

Muranishi, Critical Reviews in Therapeutic Drug Carrier Systems, 1990, 7, 1-33; Yamamoto *et al.*, J. Pharm. Exp. Ther., 1992, 263, 25; Yamashita *et al.*, J. Pharm. Sci., 1990, 79, 579-583).

Chelating agents, as used in connection with the present disclosure, can be defined as compounds that remove metallic ions from solution by forming complexes therewith, with the result that absorption of iRNAs through the mucosa is enhanced. With regards to their use as penetration enhancers in the present disclosure, chelating agents have the added advantage of also serving as DNase inhibitors, as most characterized DNA nucleases require a divalent metal ion for catalysis and are thus inhibited by chelating agents (Jarrett, J. Chromatogr., 1993, 618, 315-339). Suitable chelating agents include but are not limited to disodium ethylenediaminetetraacetate (EDTA), citric acid, salicylates (*e.g.*, sodium salicylate, 5-methoxysalicylate and homovanilate), N-acyl derivatives of collagen, laureth-9 and N-amino acyl derivatives of beta-diketones (enamines)(see *e.g.*, Katdare, A. *et al.*, Excipient development for pharmaceutical, biotechnology, and drug delivery, CRC Press, Danvers, MA, 2006; Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, page 92; Muranishi, Critical Reviews in Therapeutic Drug Carrier Systems, 1990, 7, 1-33; Buur *et al.*, J. Control Rel., 1990, 14, 43-51).

As used herein, non-chelating non-surfactant penetration enhancing compounds can be defined as compounds that demonstrate insignificant activity as chelating agents or as surfactants but that nonetheless enhance absorption of iRNAs through the alimentary mucosa (see *e.g.*, Muranishi, Critical Reviews in Therapeutic Drug Carrier Systems, 1990, 7, 1-33). This class of penetration enhancers includes, for example, unsaturated cyclic ureas, 1-alkyl- and 1-alkenylazacyclo-alkanone derivatives (Lee *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems, 1991, page 92); and non-steroidal anti-inflammatory agents such as diclofenac sodium, indomethacin and phenylbutazone (Yamashita *et al.*, J. Pharm. Pharmacol., 1987, 39, 621-626).

Agents that enhance uptake of iRNAs at the cellular level can also be added to the pharmaceutical and other compositions of the present disclosure. For example, cationic lipids, such as lipofectin (Junichi *et al*, U.S. Pat. No. 5,705,188), cationic glycerol derivatives, and polycationic molecules, such as polylysine (Lollo *et al.*, PCT Application WO 97/30731), are also known to enhance the cellular uptake of dsRNAs. Examples of commercially available transfection reagents include, for example Lipofectamine™ (Invitrogen; Carlsbad, CA), Lipofectamine 2000™ (Invitrogen; Carlsbad, CA), 293fectin™ (Invitrogen; Carlsbad, CA), Cellfectin™ (Invitrogen; Carlsbad, CA), DMRIE-C™ (Invitrogen; Carlsbad, CA), FreeStyle™ MAX (Invitrogen; Carlsbad, CA), Lipofectamine™ 2000 CD (Invitrogen; Carlsbad, CA), Lipofectamine™ (Invitrogen; Carlsbad, CA), RNAiMAX (Invitrogen; Carlsbad, CA), Oligofectamine™ (Invitrogen; Carlsbad, CA), Optifect™ (Invitrogen; Carlsbad, CA), X-tremeGENE Q2 Transfection Reagent (Roche; Grenzacherstrasse, Switzerland), DOTAP Liposomal Transfection Reagent (Grenzacherstrasse, Switzerland), DOSPER Liposomal Transfection Reagent (Grenzacherstrasse, Switzerland), or Fugene (Grenzacherstrasse,

Switzerland), Transfectam® Reagent (Promega; Madison, WI), TransFast™ Transfection Reagent (Promega; Madison, WI), Tfx™-20 Reagent (Promega; Madison, WI), Tfx™-50 Reagent (Promega; Madison, WI), DreamFect™ (OZ Biosciences; Marseille, France), EcoTransfect (OZ Biosciences; Marseille, France), TransPass[a] D1 Transfection Reagent (New England Biolabs; Ipswich, MA, USA), LyoVec™/LipoGen™ (Invitrogen; San Diego, CA, USA), PerFectin Transfection Reagent (Genlantis; San Diego, CA, USA), NeuroPORTER Transfection Reagent (Genlantis; San Diego, CA, USA), GenePORTER Transfection reagent (Genlantis; San Diego, CA, USA), GenePORTER 2 Transfection reagent (Genlantis; San Diego, CA, USA), Cytofectin Transfection Reagent (Genlantis; San Diego, CA, USA), BaculoPORTER Transfection Reagent (Genlantis; San Diego, CA, USA), TroganPORTER™ transfection Reagent (Genlantis; San Diego, CA, USA), RiboFect (Bioline; Taunton, MA, USA), PlasFect (Bioline; Taunton, MA, USA), UniFECTOR (B-Bridge International; Mountain View, CA, USA), SureFECTOR (B-Bridge International; Mountain View, CA, USA), or HiFect™ (B-Bridge International, Mountain View, CA, USA), among others.

Other agents can be utilized to enhance the penetration of the administered nucleic acids, including glycols such as ethylene glycol and propylene glycol, pyrrols such as 2-pyrrol, azones, and terpenes such as limonene and menthone.

v. Carriers

Certain compositions of the present disclosure also incorporate carrier compounds in the formulation. As used herein, "carrier compound" or "carrier" can refer to a nucleic acid, or analog thereof, which is inert (*i.e.*, does not possess biological activity per se) but is recognized as a nucleic acid by *in vivo* processes that reduce the bioavailability of a nucleic acid having biological activity by, for example, degrading the biologically active nucleic acid or promoting its removal from circulation. The coadministration of a nucleic acid and a carrier compound, typically with an excess of the latter substance, can result in a substantial reduction of the amount of nucleic acid recovered in the liver, kidney or other extracirculatory reservoirs, presumably due to competition between the carrier compound and the nucleic acid for a common receptor. For example, the recovery of a partially phosphorothioate dsRNA in hepatic tissue can be reduced when it is coadministered with polyinosinic acid, dextran sulfate, polycytidic acid or 4-acetamido-4'isothiocyano-stilbene-2,2'-disulfonic acid (Miyao *et al.*, DsRNA Res. Dev., 1995, 5, 115-121; Takakura *et al.*, DsRNA & Nucl. Acid Drug Dev., 1996, 6, 177-183.

vi. Excipients

In contrast to a carrier compound, a "pharmaceutical carrier" or "excipient" is a pharmaceutically acceptable solvent, suspending agent or any other pharmacologically inert vehicle for delivering one or more nucleic acids to an animal. The excipient can be liquid or solid and is selected, with the planned manner of administration in mind, so as to provide for the desired bulk, consistency, *etc.*, when combined with a nucleic acid and the other components of a given pharmaceutical composition. Typical pharmaceutical carriers

include, but are not limited to, binding agents (*e.g.*, pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose, *etc.*); fillers (*e.g.*, lactose and other sugars, microcrystalline cellulose, pectin, gelatin, calcium sulfate, ethyl cellulose, polyacrylates or calcium hydrogen phosphate, *etc.*); lubricants (*e.g.*, magnesium stearate, talc, silica, colloidal silicon dioxide, stearic acid, metallic stearates, hydrogenated vegetable oils, corn starch, polyethylene glycols, sodium benzoate, sodium acetate, *etc.*); disintegrants (*e.g.*, starch, sodium starch glycolate, *etc.*); and wetting agents (*e.g.*, sodium lauryl sulphate, *etc*).

Pharmaceutically acceptable organic or inorganic excipients suitable for non-parenteral administration which do not deleteriously react with nucleic acids can also be used to formulate the compositions of the present disclosure. Suitable pharmaceutically acceptable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

Formulations for topical administration of nucleic acids can include sterile and non-sterile aqueous solutions, non-aqueous solutions in common solvents such as alcohols, or solutions of the nucleic acids in liquid or solid oil bases. The solutions can also contain buffers, diluents and other suitable additives. Pharmaceutically acceptable organic or inorganic excipients suitable for non-parenteral administration which do not deleteriously react with nucleic acids can be used.

Suitable pharmaceutically acceptable excipients include, but are not limited to, water, salt solutions, alcohol, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, hydroxymethylcellulose, polyvinylpyrrolidone and the like.

vii. *Other Components*

The compositions of the present disclosure can additionally contain other adjunct components conventionally found in pharmaceutical compositions, at their art-established usage levels. Thus, for example, the compositions can contain additional, compatible, pharmaceutically-active materials such as, for example, antipruritics, astringents, local anesthetics or anti-inflammatory agents, or can contain additional materials useful in physically formulating various dosage forms of the compositions of the present disclosure, such as dyes, flavoring agents, preservatives, antioxidants, opacifiers, thickening agents and stabilizers. However, such materials, when added, should not unduly interfere with the biological activities of the components of the compositions of the present disclosure. The formulations can be sterilized and, if desired, mixed with auxiliary agents, *e.g.*, lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, colorings, flavorings and/or aromatic substances and the like which do not deleteriously interact with the nucleic acid(s) of the formulation.

Aqueous suspensions can contain substances which increase the viscosity of the suspension including, for example, sodium carboxymethylcellulose, sorbitol and/or dextran. The suspension can also contain stabilizers.

In some embodiments, pharmaceutical compositions featured in the disclosure include (a) one or more RNAi agents and (b) one or more agents which function by a non-RNAi mechanism and which are useful in treating a GRB14-associated disorder, e.g., type 1 diabetes, type 2 diabetes, prediabetes, insulin resistance, or diabetes-related conditions such as obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc. Examples of such agents include, but are not limited to, insulin (e.g., insulin detemir (Levemir), insulin glargine (Lantus)), Metformin (Glucophage), sulfonylureas, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, SGLT2 inhibitors, glucagon-like peptide-1 analogs, angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), Aliskiren (Tekturna, Rasilez), corticosteroids, protease inhibitors, orlistat (Alli, Xenical), phentermine and topiramate (Qsymia), bupropion and naltrexone (Contrave), liraglutide (Saxenda, Victoza), agents that decrease or otherwise affect the GRB14 activity, or agents that independently contribute to amelioration of symptoms and improvement of patients having a GRB14-associated disorder.

Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD_{50}/ED_{50}. Compounds that exhibit high therapeutic indices are preferred.

The data obtained from cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of compositions featured herein in the disclosure lies generally within a range of circulating concentrations that include the ED_{50} with little or no toxicity. The dosage can vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the methods featured in the disclosure, the therapeutically effective dose can be estimated initially from cell culture assays. A dose can be formulated in animal models to achieve a circulating plasma concentration range of the compound or, when appropriate, of the polypeptide product of a target sequence (*e.g.*, achieving a decreased concentration of the polypeptide) that includes the IC_{50} (*i.e.*, the concentration of the test compound which achieves a half-maximal inhibition of symptoms) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma can be measured, for example, by high performance liquid chromatography.

In addition to their administration, as discussed above, the iRNAs featured in the disclosure can be administered in combination with other known agents effective in treatment of pathological processes mediated by GRB14 expression. In any event, the administering physician can adjust the amount and timing of iRNA administration on the basis of results observed using standard measures of efficacy known in the art or described herein.

In some embodiments, the methods featured in the disclosure may utilize protecting groups. Protecting group methodology is well known to those skilled in the art (*see, for example*, PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, Green, T.W. *et al.*, Wiley-Interscience, New York City, 1999). Briefly, protecting groups within the context of this disclosure are any group that reduces or eliminates unwanted reactivity of a functional group. A protecting group can be added to a functional group to mask its reactivity during certain reactions and then removed to reveal the original functional group. In some embodiments an "alcohol protecting group" is used. An "alcohol protecting group" is any group which decreases or eliminates unwanted reactivity of an alcohol functional group. Protecting groups can be added and removed using techniques well known in the art.

VII. Methods of the Disclosure

The present disclosure also provides methods of using an iRNA of the disclosure and/or a composition of the disclosure to reduce and/or inhibit GRB14 expression in a cell, such as a cell in a subject, *e.g.*, a hepatocyte. The methods include contacting the cell with an RNAi agent or pharmaceutical composition comprising an iRNA agent of the disclosure. In some embodiments, the cell is maintained for a time sufficient to obtain degradation of the mRNA transcript of a GRB14 gene.

Reduction in gene expression can be assessed by any methods known in the art. For example, a reduction in the expression of GRB14 may be determined by determining the mRNA expression level of GRB14 using methods routine to one of ordinary skill in the art, *e.g.*, Northern blotting, qRT-PCR; by determining the protein level of GRB14 using methods routine to one of ordinary skill in the art, such as Western blotting, immunological techniques. A reduction in the expression of GRB14 may also be assessed indirectly by measuring a decrease in biological activity of GRB14, *e.g.*, a decrease in the enzymatic activity of GRB14 and/or a change in one or more associated markers of GRB14 activity (e.g., insulin receptor levels, glucose levels, HbA1c levels, etc.).

In the methods of the disclosure the cell may be contacted *in vitro* or *in vivo, i.e.*, the cell may be within a subject.

A cell suitable for treatment using the methods of the disclosure may be any cell that expresses a GRB14 gene. A cell suitable for use in the methods of the disclosure may be a mammalian cell, *e.g.*, a primate cell (such as a human cell or a non-human primate cell, *e.g.*, a monkey cell or a chimpanzee cell), a non-primate cell (such as a cow cell, a pig cell, a camel cell, a llama cell, a horse cell, a goat cell, a rabbit cell, a sheep cell, a hamster, a guinea pig cell, a cat cell, a dog cell, a rat cell, a mouse cell, a lion cell, a tiger cell, a bear cell, or a buffalo cell), a bird cell (*e.g.*, a duck cell or a goose cell), or a whale cell. In one embodiment, the cell is a human cell, *e.g.*, a human liver cell.

GRB14 expression is inhibited in the cell by at least about 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or about 100%. In preferred embodiments, GRB14 expression is inhibited by at least 20%.

In one embodiment, the *in vivo* methods of the disclosure may include administering to a subject a composition containing an iRNA, where the iRNA includes a nucleotide sequence that is complementary to at least a part of an RNA transcript of the GRB14 gene of the mammal to be treated.

When the organism to be treated is a mammal such as a human, the composition can be administered by any means known in the art including, but not limited to oral, intraperitoneal, or parenteral routes, including intracranial (*e.g.*, intraventricular, intraparenchymal and intrathecal), intravenous, intramuscular, subcutaneous, transdermal, airway (aerosol), nasal, rectal, and topical (including buccal and sublingual) administration. In certain embodiments, the compositions are administered by intravenous infusion or injection. In certain embodiments, the compositions are administered by subcutaneous injection.

In some embodiments, the administration is *via* a depot injection. A depot injection may release the iRNA in a consistent way over a prolonged time period. Thus, a depot injection may reduce the frequency of dosing needed to obtain a desired effect, *e.g.*, a desired inhibition of GRB14, or a therapeutic or prophylactic effect. A depot injection may also provide more consistent serum concentrations. Depot injections may include subcutaneous injections or intramuscular injections. In preferred embodiments, the depot injection is a subcutaneous injection.

In some embodiments, the administration is *via* a pump. The pump may be an external pump or a surgically implanted pump. In certain embodiments, the pump is a subcutaneously implanted osmotic pump. In other embodiments, the pump is an infusion pump. An infusion pump may be used for intravenous, subcutaneous, arterial, or epidural infusions. In preferred embodiments, the infusion pump is a subcutaneous infusion pump. In other embodiments, the pump is a surgically implanted pump that delivers the iRNA to the liver.

An iRNA of the disclosure may be present in a pharmaceutical composition, such as in a suitable buffer solution. The buffer solution may comprise acetate, citrate, prolamine, carbonate, or phosphate, or any combination thereof. In one embodiment, the buffer solution is phosphate buffered saline (PBS). The pH and osmolarity of the buffer solution containing the iRNA can be adjusted such that it is suitable for administering to a subject.

Alternatively, an iRNA of the disclosure may be administered as a pharmaceutical composition, such as a dsRNA liposomal formulation.

The mode of administration may be chosen based upon whether local or systemic treatment is desired and based upon the area to be treated. The route and site of administration may be chosen to enhance targeting.

In one aspect, the present disclosure also provides methods for inhibiting the expression of a GRB14 gene in a mammal. The methods include administering to the mammal a composition comprising a dsRNA that targets a GRB14 gene in a cell of the mammal, thereby inhibiting expression of the GRB14 gene in the cell.

In some embodiment, the methods include administering to the mammal a composition comprising a dsRNA that targets a GRB14 gene in a cell of the mammal, thereby inhibiting expression of the GRB14 gene in the cell.

In another aspect, the present disclosure provides use of an iRNA agent or a pharmaceutical composition of the disclosure for inhibiting the expression of a GRB14 gene in a mammal.

In yet another aspect, the present disclosure provides use of an iRNA agent of the disclosure targeting a GRB14 gene or a pharmaceutical composition comprising such an agent in the manufacture of a medicament for inhibiting expression of a GRB14 gene in a mammal.

Reduction in gene expression can be assessed by any methods known it the art and by methods, *e.g.* qRT-PCR, described herein. Reduction in protein production can be assessed by any methods known it the art and by methods, *e.g.* ELISA, enzymatic activity, described herein.

The present disclosure also provides therapeutic and prophylactic methods which include administering to a subject having, or prone to developing a fatty liver-associated disease, disorder, or condition, the iRNA agents, pharmaceutical compositions comprising an iRNA agent, or vectors comprising an iRNA of the disclosure.

In one aspect, the present disclosure provides methods of treating a subject having a disorder that would benefit from reduction in GRB14 expression, *e.g.*, a GRB14-associated disease.

The treatment methods (and uses) of the disclosure include administering to the subject, *e.g.*, a human, a therapeutically effective amount of a dsRNA agent that inhibits expression of GRB14 or a pharmaceutical composition comprising a dsRNA that inhibits expression of GRB14, thereby treating the subject.

In one aspect, the disclosure provides methods of preventing at least one symptom in a subject having a disorder that would benefit from reduction in GRB14 expression, *e.g.*, diabetes. The methods include administering to the subject a prophylactically effective amount of dsRNA agent or a pharmaceutical composition comprising a dsRNA, thereby preventing at least one symptom in the subject. In one embodiment, the at least one symptom is a symptom of a GRB14-associated disease.

The present disclosure also provides use of a therapeutically effective amount of an iRNA agent of the disclosure or a pharmaceutical composition comprising a dsRNA that inhibits expression of GRB14 for

treating a subject, *e.g.*, a subject that would benefit from a reduction and/or inhibition of GRB14 expression, *e.g.*, a GRB14-associated disease, *e.g.*, diabetes.

In another aspect, the present disclosure provides use of an iRNA agent, *e.g.*, a dsRNA, of the disclosure targeting a GRB14 for gene or a pharmaceutical composition comprising an iRNA agent targeting a GRB14 for gene in the manufacture of a medicament for treating a subject, *e.g.*, a subject that would benefit from a reduction and/or inhibition of GRB14 for expression, *e.g.*, a GRB14-associated disease.

The present disclosure also provides use of a prophylactically effective amount of an iRNA agent of the disclosure or a pharmaceutical composition comprising a dsRNA that inhibits expression of GRB14 for preventing at least one symptom in a subject having a disorder that would benefit from reduction in GRB14 expression, *e.g.*, diabetes.

In another aspect, the present disclosure provides use of an iRNA agent, *e.g.*, a dsRNA, of the disclosure targeting a GRB14 gene or a pharmaceutical composition comprising an iRNA agent targeting a GRB14 gene in the manufacture of a medicament for preventing at least one symptom in a subject having a disorder that would benefit from reduction in GRB14 expression, *e.g.*, diabetes.

Accordingly, in one aspect, the present disclosure provides methods of treating a subject having a disorder that would benefit from reduction in GRB14 expression, *e.g.*, a GRB14-associated disease, such as diabetes. In one embodiment, the GRB14-associated disease is type 2 diabetes. In one embodiment, the GRB14-associated disease is type 1 diabetes. In one embodiment, the GRB14-associated disease is prediabetes. In one embodiment, the GRB14-associated disease is insulin resistance. In one embodiment, the GRB14-associated disease is a diabetes-related condition such as obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, stroke, etc.

In another embodiment, the subject is homozygous for the GRB14 gene. Each allele of the gene may encode a functional GRB14 protein. In yet another embodiment, the subject is heterozygous for the GRB14 gene. The subject may have an allele encoding a functional GRB14 protein and an allele encoding a loss of function variant of GRB14. In some embodiments, the subject has an allele encoding the rs3923113 variant. In some ebomdiments, the subject has an allele encoding the rs10195252 variant.

In some embodiments, the subject has a GIGYF1 loss of function allele. In some embodiments, the subject has a GIGYF1 rs221797 variant (e.g., rs221797:A). In some embodiments, the subject has a GIGYF1 rs117231629 variant. In some embodiments, the subject has a GIGYF2 loss of function allele. In some embodiments, the subject has a GIGYF2 rs1801251 variant (e.g., rs1801251:A).

In one embodiment, a GRB14-associated disorder is type 2 diabetes (T2D), used interchangeably with type 2 diabetes mellitus (2DM) or type II diabetes. Type 2 diabetes is a chronic multifactorial polygenic disease, influenced by multilple genes and environmental factors, characterized by impaired glucose

intolerance due to insulin resistance or relative insulin deficiency. In the progression of diabetes, insulin secretion is increased, and a large amount of the increase in the first stage of this compensation process is due to increased β-cell mass, which is mainly achieved through an increase in β-cell number. Eventually, insulin targets such as liver, muscle and adipose tissues become insulin-resistant and pancreatic β-cells show impaired insulin secretion. Progression from normal glucose tolerance to impaired glucose tolerance to type 2 diabetes is characterized by a progressive decline in insulin secretion and plasma insulin concentration and a progressive rise in plasma glucagon concentration. Type 2 diabetic patients are also characterized by hyperglucagonaemia and enhanced hepatic glucose production in response to glucagon as the suppression of glucose production is decreased. Excessive glucose production and lipid accumulation are observed in the livers of obese patients with insulin resistance. Excessive hepatic glucose production drives hyperglycemia. Symptoms and signs of type 2 diabetes include increased thirst, frequent urination, increased hunger, fatigue, blurred vision, slow-healing sores, frequent infections, and areas of darkened skin. Uncontrolled type 2 diabetes leads to serious complications including diabetic retinopathy, diabetic vasculopathy, diabetic neuropathy, and diabetic nephropathy. Being overweight or obese is a major modifiable risk factor for type 2 diabetes, and other risk factors include physical inactivity and family history. Early stage type 2 diabetes may be controlled by dietary regimen and weight loss. In advanced stages, type 2 diabetes can be treated by medication (e.g., metformin, sulfonylureas, meglitinides) or insulin injection.

In one embodiment, a GRB14-associated disorder is type 1 diabetes (T1D), also known as juvenile diabetes. Type 1 diabetes is a polygenic disease that is highly heritable and ischaracterized by no production or insufficient production of insulin by the pancreas. While the cause of type 1 diabetes is unknown, the pathophysiology involves an autoimmune destruction of the insulin-producing β-cells in the pancreas. The classic symptoms are frequent urination, increased thirst, increased hunger, and weight loss, and may include blurry vision, tiredness, and poor wound healing. Symptoms typically develop over a short period of time. Uncontrolled type 1 diabetes can lead to complications including ketoacidosis, cardiovascular disease, diabetic neuropathy, diabetic retinopathy, sexual dysfunction, and a high prevalence of urinary tract infections. Insulin injections are generally necessary for the control of type 1 diabetes.

In one embodiment, a GRB14-associated disorder is prediabetes. Prediabetes may be characterized by elevated blood glucose levels that are below the threshold for type 2 diabetes, but may be an early stage of disease that progresses to type 2 diabetes. Subjects having prediabetes often have obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension. Subjects with prediabetes may be at increased risk of cardiovascular disease and/or of developing type 2 diabetes.

In one embodiment, a GRB14-associated disorder is insulin resistance. Insulin resistance is not entirely understood, but is characterized by reduced sensitivity of insulin-targeting tissues to insulin resulting

in the inability of insulin to properly regulate glucose transport and blood glucose levels. Insulin resistance is a component of type 2 diabetes and may be a component of prediabetes. Risk factors for insulin resistance include obesity, a sedentary lifestyle, and hereditary factors. Insulin resistance can generally be improved with lifestyle modifications, including diet and exercise.

In one embodiment, an "iRNA" for use in the methods of the disclosure is a "dual targeting RNAi agent." The term "dual targeting RNAi agent" refers to a molecule comprising a first dsRNA agent comprising a complex of ribonucleic acid molecules, having a duplex structure comprising two anti-parallel and substantially complementary nucleic acid strands, referred to as having "sense" and "antisense" orientations with respect to a first target RNA, *i.e.*, a GRB14 gene, covalently attached to a molecule comprising a second dsRNA agent comprising a complex of ribonucleic acid molecules, having a duplex structure comprising two anti-parallel and substantially complementary nucleic acid strands, referred to as having "sense" and "antisense" orientations with respect to a second target RNA. In some embodiments of the disclosure, a dual targeting RNAi agent triggers the degradation of the first and the second target RNAs, *e.g.*, mRNAs, through a post-transcriptional gene-silencing mechanism referred to herein as RNA interference or RNAi.

The dsRNA agent may be administered to the subject at a dose of about 0.1 mg/kg to about 50 mg/kg. Typically, a suitable dose will be in the range of about 0.1 mg/kg to about 5.0 mg/kg, preferably about 0.3 mg/kg and about 3.0 mg/kg.

The iRNA can be administered by intravenous infusion over a period of time, on a regular basis. In certain embodiments, after an initial treatment regimen, the treatments can be administered on a less frequent basis.

Administration of the iRNA can reduce GRB14 levels, *e.g.*, in a cell, tissue, blood, urine or other compartment of the patient by at least about 5%, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 39, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or at least about 99% or more. In a preferred embodiment, administration of the iRNA can reduce GRB14 levels, *e.g.*, in a cell, tissue, blood, urine or other compartment of the patient by at least 20%.

Before administration of a full dose of the iRNA, patients can be administered a smaller dose, such as a 5% infusion reaction, and monitored for adverse effects, such as an allergic reaction. In another example, the patient can be monitored for unwanted immunostimulatory effects, such as increased cytokine (*e.g.*, TNF-alpha or INF-alpha) levels.

Alternatively, the iRNA can be administered subcutaneously, *i.e.*, by subcutaneous injection. One or more injections may be used to deliver the desired daily dose of iRNA to a subject. The injections may be

repeated over a period of time. The administration may be repeated on a regular basis. In certain embodiments, after an initial treatment regimen, the treatments can be administered on a less frequent basis. A repeat-dose regimen may include administration of a therapeutic amount of iRNA on a regular basis, such as every other day or to once a year. In certain embodiments, the iRNA is administered about once per week, once every 7-10 days, once every 2 weeks, once every 3 weeks, once every 4 weeks, once every 5 weeks, once every 6 weeks, once every 7 weeks, once every 8 weeks, once every 9 weeks, once every 10 weeks, once every 11 weeks, once every 12 weeks, once per month, once every 2 months, once every 3 months once per quarter), once every 4 months, once every 5 months, or once every 6 months.

In one embodiment, the method includes administering a composition featured herein such that expression of the target GRB14 gene is decreased, such as for about 1, 2, 3, 4, 5, 6, 7, 8, 12, 16, 18, 24 hours, 28, 32, or about 36 hours. In one embodiment, expression of the target GRB14 gene is decreased for an extended duration, *e.g.*, at least about two, three, four days or more, *e.g.*, about one week, two weeks, three weeks, or four weeks or longer.

Preferably, the iRNAs useful for the methods and compositions featured herein specifically target RNAs (primary or processed) of the target GRB14 gene. Compositions and methods for inhibiting the expression of these genes using iRNAs can be prepared and performed as described herein.

Administration of the dsRNA according to the methods of the disclosure may result in a reduction of the severity, signs, symptoms, and/or markers of such diseases or disorders in a patient with a disorder of lipid metabolism. By "reduction" in this context is meant a statistically significant decrease in such level. The reduction can be, for example, at least about 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or about 100%.

Efficacy of treatment or prevention of disease can be assessed, for example by measuring disease progression, disease remission, symptom severity, reduction in pain, quality of life, dose of a medication required to sustain a treatment effect, level of a disease marker or any other measurable parameter appropriate for a given disease being treated or targeted for prevention. It is well within the ability of one skilled in the art to monitor efficacy of treatment or prevention by measuring any one of such parameters, or any combination of parameters. For example, efficacy of treatment of diabetes may be assessed, for example, by periodic monitoring of glucose levels or HbA1c levels. Comparisons of the later readings with the initial readings provide a physician an indication of whether the treatment is effective. It is well within the ability of one skilled in the art to monitor efficacy of treatment or prevention by measuring any one of such parameters, or any combination of parameters. In connection with the administration of an iRNA or pharmaceutical composition thereof, "effective against" a disorder indicates that administration in a clinically appropriate manner results in a beneficial effect for at least a statistically significant fraction of patients having the disorder, such as an improvement of symptoms, a cure, a reduction in disease, extension of life, improvement

in quality of life, or other effect generally recognized as positive by medical doctors familiar with treating the disorder (*e.g.*, diabetes) and the related causes.

A treatment or preventive effect is evident when there is a statistically significant improvement in one or more parameters of disease status, or by a failure to worsen or to develop symptoms where they would otherwise be anticipated. As an example, a favorable change of at least 10% in a measurable parameter of disease, and preferably at least 20%, 30%, 40%, 50% or more can be indicative of effective treatment. Efficacy for a given iRNA drug or formulation of that drug can also be judged using an experimental animal model for the given disease as known in the art.

The iRNA agent and an additional therapeutic agent and/or treatment may be administered at the same time and/or in the same combination, *e.g.*, subcutaneously, or the additional therapeutic agent can be administered as part of a separate composition or at separate times and/or by another method known in the art or described herein.

VIII. Kits

The present disclosure also provides kits for performing any of the methods of the disclosure. Such kits include one or more RNAi agent(s) and instructions for use, *e.g.*, instructions for inhibiting expression of a GRB14 in a cell by contacting the cell with an RNAi agent or pharmaceutical composition of the disclosure in an amount effective to inhibit expression of the GRB14. The kits may optionally further comprise means for contacting the cell with the RNAi agent (*e.g.*, an injection device), or means for measuring the inhibition of GRB14 (*e.g.*, means for measuring the inhibition of GRB14 mRNA and/or GRB14 protein). Such means for measuring the inhibition of GRB14 may comprise a means for obtaining a sample from a subject, such as, e.g., a plasma sample. The kits of the disclosure may optionally further comprise means for administering the RNAi agent(s) to a subject or means for determining the therapeutically effective or prophylactically effective amount.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the iRNAs and methods featured in the disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

EXAMPLES

Example 1. GRB14 iRNA Design, Synthesis, and Selection

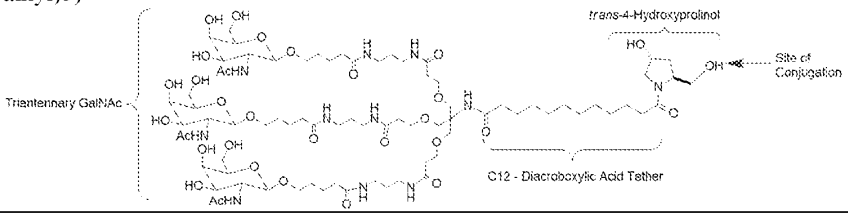
This Example describes methods for the design, synthesis, and selection of GRB14 iRNA agents.

Nucleic acid sequences provided herein are represented using standard nomenclature. *See* the abbreviations of Table 1.

Table 1. Abbreviations of nucleotide monomers used in nucleic acid sequence representation

It will be understood that these monomers, when present in an oligonucleotide, are mutually linked by 5'-3'-phosphodiester bonds.

Abbreviation	Nucleotide(s)
A	Adenosine-3'-phosphate
Af	2'-fluoroadenosine-3'-phosphate
Afs	2'-fluoroadenosine-3'-phosphorothioate
As	adenosine-3'-phosphorothioate
C	cytidine-3'-phosphate
Cf	2'-fluorocytidine-3'-phosphate
Cfs	2'-fluorocytidine-3'-phosphorothioate
Cs	cytidine-3'-phosphorothioate
G	guanosine-3'-phosphate
Gf	2'-fluoroguanosine-3'-phosphate
Gfs	2'-fluoroguanosine-3'-phosphorothioate
Gs	guanosine-3'-phosphorothioate
T	5'-methyluridine-3'-phosphate
Tf	2'-fluoro-5-methyluridine-3'-phosphate
Tfs	2'-fluoro-5-methyluridine-3'-phosphorothioate
Ts	5-methyluridine-3'-phosphorothioate
U	Uridine-3'-phosphate
Uf	2'-fluorouridine-3'-phosphate
Ufs	2'-fluorouridine -3'-phosphorothioate
Us	uridine -3'-phosphorothioate
N	any nucleotide (G, A, C, T or U)
a	2'-O-methyladenosine-3'-phosphate
as	2'-O-methyladenosine-3'- phosphorothioate
c	2'-O-methylcytidine-3'-phosphate
cs	2'-O-methylcytidine-3'- phosphorothioate
g	2'-O-methylguanosine-3'-phosphate
gs	2'-O-methylguanosine-3'- phosphorothioate
t	2'-O-methyl-5-methyluridine-3'-phosphate
ts	2'-O-methyl-5-methyluridine-3'-phosphorothioate
u	2'-O-methyluridine-3'-phosphate
us	2'-O-methyluridine-3'-phosphorothioate
s	phosphorothioate linkage

Abbreviation	Nucleotide(s)
L96[1]	N-[tris(GalNAc-alkyl)-amidodecanoyl)]-4-hydroxyprolinol (Hyp-(GalNAc-alkyl)3) 
P	Phosphate
VP	Vinyl-phosphonate
dA	2`-deoxyadenosine-3`-phosphate
dAs	2`-deoxyadenosine-3`-phosphorothioate
dC	2`-deoxycytidine-3`-phosphate
dCs	2`-deoxycytidine-3`-phosphorothioate
dG	2`-deoxyguanosine-3`-phosphate
dGs	2`-deoxyguanosine-3`-phosphorothioate
dT	2`-deoxythymidine-3`-phosphate
dTs	2`-deoxythymidine-3`-phosphorothioate
dU	2`-deoxyuridine
dUs	2`-deoxyuridine-3`-phosphorothioate
Y34	2-hydroxymethyl-tetrahydrofuran-4-methoxy-3-phosphate (abasic 2`-OMe furanose)
Y44	inverted abasic DNA (2-hydroxymethyl-tetrahydrofuran-5-phosphate)
(Agn)	Adenosine-glycol nucleic acid (GNA)
(Cgn)	Cytidine-glycol nucleic acid (GNA)
(Ggn)	Guanosine-glycol nucleic acid (GNA)
(Tgn)	Thymidine-glycol nucleic acid (GNA) S-Isomer

Experimental Methods

Bioinformatics

Source of reagents

Where the source of a reagent is not specifically given herein, such reagent can be obtained from any supplier of reagents for molecular biology at a quality/purity standard for application in molecular biology.

Transcripts

A set of siRNAs targeting the human growth factor receptor bound protein 14 (GRB14) gene (human NCBI refseqID NM_004490.3; NCBI GeneID: 2888) were designed using custom R and Python scripts. All the GRB14 siRNA designs have a perfect match to the human GRB14 transcript (transcript variant 1). The human NM_004490 REFSEQ mRNA, version 3, has a length of 2,415 bases.

siRNA Synthesis

siRNAs were synthesized and annealed using routine methods known in the art.

Briefly, siRNA sequences were synthesized at 1 μmol scale on a Mermade 192 synthesizer (BioAutomation) using the solid support mediated phosphoramidite chemistry. The solid support was controlled pore glass (500 A) loaded with custom GalNAc ligand or universal solid support (AM biochemical). Ancillary synthesis reagents, 2'-F and 2'-O-Methyl RNA and deoxy phosphoramidites were obtained from Thermo-Fisher (Milwaukee, WI) and Hongene (China). 2'F 2'-O-Methyl, GNA (glycol nucleic acids), 5'-phosphate and other modifications were introduced using the corresponding phosphoramidites. For all the duplex designs shown in Table 3, a 5'-phosphate was introduced at the 5' nucleotide position of the antisense strand. Synthesis of 3' GalNAc conjugated single strands was performed on a GalNAc modified CPG support. Custom CPG universal solid support was used for the synthesis of antisense single strands. Coupling time for all phosphoramidites (100 mM in acetonitrile) was 5 min employing 5-Ethylthio-1H-tetrazole (ETT) as activator (0.6 M in acetonitrile). Phosphorothioate linkages were generated using a 50 mM solution of 3-((Dimethylamino-methylidene) amino)-3H-1,2,4-dithiazole-3-thione (DDTT, obtained from Chemgenes (Wilmington, MA, USA)) in anhydrous acetonitrile/pyridine (1:1 v/v). Oxidation time was 3 minutes. All sequences were synthesized with final removal of the DMT group ("DMT off").

Upon completion of the solid phase synthesis, oligoribonucleotides were cleaved from the solid support and deprotected in sealed 96 deep well plates using 200 μL Aqueous Methylamine reagents at 60°C for 20 minutes. For sequences containing 2' ribo residues (2'-OH) that are protected with a tert-butyl dimethyl silyl (TBDMS) group, a second step deprotection was performed using TEA.3HF (triethylamine trihydro fluoride) reagent. To the methylamine deprotection solution, 200uL of dimethyl sulfoxide (DMSO) and 300ul TEA.3HF reagent was added and the solution was incubated for additional 20min at 60°C. At the end of cleavage and deprotection step, the synthesis plate was allowed to come to room temperature and was precipitated by addition of 1mL of acetontile: ethanol mixture (9:1). The plates were cooled at -80 C for 2 hrs, supernatant decanted carefully with the aid of a multi-channel pipette. The oligonucleotide pellet was re-suspended in 20mM NaOAc buffer and were desalted using a 5 mL HiTrap size exclusion column (GE Healthcare) on an AKTA Purifier System equipped with an A905 autosampler and a Frac 950 fraction collector. Desalted samples were collected in 96-well plates. Samples from each sequence were analyzed by LC-MS to confirm the identity, UV (260 nm) for quantification and a selected set of samples by IEX chromatography to determine purity.

Annealing of single strands was performed on a Tecan liquid handling robot. Equimolar mixture of sense and antisense single strands were combined and annealed in 96 well plates. After combining the complementary single strands, the 96-well plate was sealed tightly and heated in an oven at 100°C for 10 minutes and allowed to come slowly to room temperature over a period 2-3 hours. The concentration of each duplex was normalized to 10μM in 1X PBS and then submitted for *in vitro* screening assays.

Detailed lists of the unmodified nucleotide sequences of the sense strand and antisense strand sequences for dsRNA agents targeting GRB14 are shown in Table 2. Detailed lists of the modified nucleotide sequences of the sense strand and antisense strand sequences for dsRNA agents targeting GRB14 are shown in Table 3. Unmodified and modified nucleotide sequences of the sense strand and antisense strand sequences designed with a VP at the 5' end of the antisense strand for dsRNA agents targeting GRB14 are shown in Tables 4 and 5, respectively. Unmodified and modified nucleotide sequences of the sense strand and antisense strand sequences designed without a VP at the 5' end of the antisense strand for dsRNA agents targeting GRB14 are shown in Tables 6 and 7, respectively.

It is to be understood that, throughout the application, a duplex name without a decimal is equivalent to a duplex name with a decimal, which merely references the batch number of the duplex. For example, AD-2217262 is equivalent to AD-2217262.1.

Table 2. Human Unmodified Sense and Antisense Strand Sequences of GRB14 dsRNA Agents

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1947923	GCGACAAUGACCACUUCCCUU	25	168-188	AAGGGAAGUGGTCAUUGUCGCCG	1506	166-188
AD-1947924	GCGACAAUGACCACUUCCCUU	26	168-188	AAGGGAAGUGGUCAUUGUCGCCG	1507	166-188
AD-1947925	GACAAUGACCACUUCCCUGCU	27	170-190	AGCAGGGAAGUGGUCAUUGUCGC	1508	168-190
AD-1947926	ACAAUGACCACUUCCCUGCAU	28	171-191	ATGCAGGGAAGTGGUCAUUGUCG	1509	169-191
AD-1947927	CAAUGACCACUUCCCUGCAAU	29	172-192	ATUGCAGGGAAGUGGUCAUUGUC	1510	170-192
AD-1947928	AAUGACCACUUCCCUGCAAGU	30	173-193	ACUUGCAGGGAAGUGGUCAUUGU	1511	171-193
AD-1947929	AAUGACCACUUCCCUGCAAGU	31	173-193	ACUUGCAGGGAAGUGGUCAUUGU	1512	171-193
AD-1947930	UGACCACUUCCCUGCAAGAUU	32	175-195	AAUCTUGCAGGGAAGUGGUCAUU	1513	173-195
AD-1947931	GACCACUUCCCUGCAAGAUGU	33	176-196	ACAUCUTGCAGGGAAGUGGUCAU	1514	174-196
AD-1947932	ACCACUUCCCUGCAAGAUGGU	34	177-197	ACCATCTUGCAGGGAAGUGGUCA	1515	175-197
AD-1947933	ACCACUUCCCUGCAAGAUGGU	35	177-197	ACCATCTUGCAGGGAAGUGGUCA	1516	175-197
AD-1947934	UUCCCUGCAAGAUGGGCAGAU	36	182-202	ATCUGCCCAUCTUGCAGGGAAGU	1517	180-202
AD-1947935	UCCCUGCAAGAUGGGCAGAGU	37	183-203	ACUCTGCCCAUCUUGCAGGGAAG	1518	181-203
AD-1947936	CCCUGCAAGAUGGGCAGAGCU	38	184-204	AGCUCUGCCCATCUUGCAGGGAA	1519	182-204

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1947937	GCUGCAGACAGG AGAAAAAAU	39	354-374	ATUUTUTCUCCTG UCUGCAGCAC	1520	352-374
AD-1947938	GCUGCAGACAGG AGAAAAAAU	40	354-374	AUUUTUTCUCCUG UCUGCAGCAC	1521	352-374
AD-1947939	CUGCAGACAGGA GAAAAAAGU	41	355-375	ACUUTUTUCUCCU GUCUGCAGCA	1522	353-375
AD-1947940	UGCAGACAGGAG AAAAAAGAU	42	356-376	ATCUTUTUUCUCC UGUCUGCAGC	1523	354-376
AD-1947941	UGCAGACAGGAG AAAAAAGAU	43	356-376	AUCUTUTUUCUCC UGUCUGCAGC	1524	354-376
AD-1947942	GCAGACAGGAGA AAAAAGAAU	44	357-377	ATUCTUTUUUCTC CUGUCUGCAG	1525	355-377
AD-1947943	GCAGACAGGAGA AAAAAGAAU	45	357-377	AUUCTUTUUUCUC CUGUCUGCAG	1526	355-377
AD-1947944	CAGACAGGAGAA AAAAGAAAU	46	358-378	ATUUCUTUUUUCU CCUGUCUGCA	1527	356-378
AD-1947945	CAGACAGGAGAA AAAAGAAAU	47	358-378	AUUUCUTUUUUC UCCUGUCUGCA	1528	356-378
AD-1947946	GACAGGAGAAAA AAGAAAGAU	48	360-380	ATCUTUCUUUUTU CUCCUGUCUG	1529	358-380
AD-1947947	ACAGGAGAAAAA AGAAAGAUU	49	361-381	AAUCTUTCUUUTU UCUCCUGUCU	1530	359-381
AD-1947948	ACAGGAGAAAAA AGAAAGAUU	50	361-381	AAUCTUTCUUUUU UCUCCUGUCU	1531	359-381
AD-1947949	CAGGAGAAAAAA GAAAGAUCU	51	362-382	AGAUCUTUCUUTU UUCUCCUGUC	1532	360-382
AD-1947950	CAGGAGAAAAAA GAAAGAUCU	52	362-382	AGAUCUTUCUUU UUUCUCCUGUC	1533	360-382
AD-1947951	AGGAGAAAAAA GAAAGAUCUU	53	363-383	AAGATCTUUCUTU UUUCUCCUGU	1534	361-383
AD-1947952	AGGAGAAAAAA GAAAGAUCUU	54	363-383	AAGATCTUUCUUU UUUCUCCUGU	1535	361-383
AD-1947953	GGAGAAAAAAG AAAGAUCUUU	55	364-384	AAAGAUCUUUCT UUUUUCUCCUG	1536	362-384
AD-1947954	GAGAAAAAAGA AAGAUCUUGU	56	365-385	ACAAGATCUUUC UUUUUUCUCCU	1537	363-385
AD-1947955	AGAAAAAAGAA AGAUCUUGAU	57	366-386	ATCAAGAUCUUTC UUUUUUCUCC	1538	364-386
AD-1947956	AGAAAAAAGAA AGAUCUUGAU	58	366-386	AUCAAGAUCUUU CUUUUUUCUCC	1539	364-386
AD-1947957	GAAAAAAGAAA GAUCUUGAUU	59	367-387	AAUCAAGAUCUT UCUUUUUUCUC	1540	365-387
AD-1947958	AAAAAAGAAAG AUCUUGAUGU	60	368-388	ACAUCAAGAUCT UUCUUUUUUCU	1541	366-388
AD-1947959	AAAAAGAAAGA UCUUGAUGUU	61	369-389	AACATCAAGAUC UUUCUUUUUUC	1542	367-389
AD-1947960	AAAAGAAAGAUC UUGAUGUUU	62	370-390	AAACAUCAAGAT CUUUCUUUUUU	1543	368-390

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1947961	AAAGAAAGAUCUUGAUGUUCU	63	371-391	AGAACATCAAGAUCUUUCUUUUU	1544	369-391
AD-1947962	AAAGAAAGAUCUUGAUGUUCU	64	371-391	AGAACATCAAGAUCUUUCUUUUU	1545	369-391
AD-1947963	AAGAAAGAUCUUGAUGUUCCU	65	372-392	AGGAACAUCAAGAUCUUUCUUUU	1546	370-392
AD-1947964	AAGAAAGAUCUUGAUGUUCCU	66	372-392	AGGAACAUCAAGAUCUUUCUUUU	1547	370-392
AD-1947965	AGAAAGAUCUUGAUGUUCCGU	67	373-393	ACGGAACAUCAAGAUCUUUCUUU	1548	371-393
AD-1947966	AAAGAUCUUGAUGUUCCGGAU	68	375-395	ATCCGGAACAUCAAGAUCUUUCU	1549	373-395
AD-1947967	AAGAUCUUGAUGUUCCGGAAU	69	376-396	ATUCCGGAACATCAAGAUCUUUC	1550	374-396
AD-1947968	AGAUCUUGAUGUUCCGGAAAU	70	377-397	ATUUCCGGAACAUCAAGAUCUUU	1551	375-397
AD-1947969	GAUCUUGAUGUUCCGGAAAUU	71	378-398	AAUUTCCGGAACAUCAAGAUCUU	1552	376-398
AD-1947970	AUCUUGAUGUUCCGGAAAUGU	72	379-399	ACAUTUCCGGAACAUCAAGAUCU	1553	377-399
AD-1947971	UCUUGAUGUUCCGGAAAUGCU	73	380-400	AGCATUTCCGGAACAUCAAGAUC	1554	378-400
AD-1947972	CUUGAUGUUCCGGAAAUGCCU	74	381-401	AGGCAUTUCCGGAACAUCAAGAU	1555	379-401
AD-1947973	CUUGAUGUUCCGGAAAUGCCU	75	381-401	AGGCAUTUCCGGAACAUCAAGAU	1556	379-401
AD-1947974	UUGAUGUUCCGGAAAUGCCAU	76	382-402	ATGGCATUUCCGGAACAUCAAGA	1557	380-402
AD-1947975	UUGAUGUUCCGGAAAUGCCAU	77	382-402	AUGGCATUUCCGGAACAUCAAGA	1558	380-402
AD-1947976	UGAUGUUCCGGAAAUGCCAUU	78	383-403	AAUGGCAUUUCCGGAACAUCAAG	1559	381-403
AD-1947977	UGAUGUUCCGGAAAUGCCAUU	79	383-403	AAUGGCAUUUCCGGAACAUCAAG	1560	381-403
AD-1947978	GAUGUUCCGGAAAUGCCAUCU	80	384-404	AGAUGGCAUUUCCGGAACAUCAA	1561	382-404
AD-1947979	AUGUUCCGGAAAUGCCAUCUU	81	385-405	AAGATGGCAUUTCCGGAACAUCA	1562	383-405
AD-1947980	UGUUCCGGAAAUGCCAUCUAU	82	386-406	ATAGAUGGCAUTUCCGGAACAUC	1563	384-406
AD-1947981	GUUCCGGAAAUGCCAUCUAUU	83	387-407	AAUAGATGGCATUUCCGGAACAU	1564	385-407
AD-1947982	GUUCCGGAAAUGCCAUCUAUU	84	387-407	AAUAGATGGCAUUUCCGGAACAU	1565	385-407
AD-1947983	UUCCGGAAAUGCCAUCUAUUU	85	388-408	AAAUAGAUGGCAUUUCCGGAACA	1566	386-408
AD-1947984	UUCCGGAAAUGCCAUCUAUUU	86	388-408	AAAUAGAUGGCAUUUCCGGAACA	1567	386-408

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1947985	UCCGGAAAUGCCAUCUAUUCU	87	389-409	AGAATAGAUGGCAUUUCCGGAAC	1568	387-409
AD-1947986	CCGGAAAUGCCAUCUAUUCCU	88	390-410	AGGAAUAGAUGGCAUUUCCGGAA	1569	388-410
AD-1947987	CGGAAAUGCCAUCUAUUCCAU	89	391-411	ATGGAATAGAUGGCAUUUCCGGA	1570	389-411
AD-1947988	CGGAAAUGCCAUCUAUUCCAU	90	391-411	AUGGAATAGAUGGCAUUUCCGGA	1571	389-411
AD-1947989	GGAAAUGCCAUCUAUUCCAAU	91	392-412	ATUGGAAUAGATGGCAUUUCCGG	1572	390-412
AD-1947990	GGAAAUGCCAUCUAUUCCAAU	92	392-412	AUUGGAAUAGAUGGCAUUUCCGG	1573	390-412
AD-1947991	GAAAUGCCAUCUAUUCCAAAU	93	393-413	ATUUGGAAUAGAUGGCAUUUCCG	1574	391-413
AD-1947992	GAAAUGCCAUCUAUUCCAAAU	94	393-413	AUUUGGAAUAGAUGGCAUUUCCG	1575	391-413
AD-1947993	AAAUGCCAUCUAUUCCAAACU	95	394-414	AGUUTGGAAUAGAUGGCAUUUCC	1576	392-414
AD-1947994	AAUGCCAUCUAUUCCAAACCU	96	395-415	AGGUTUGGAAUAGAUGGCAUUUC	1577	393-415
AD-1947995	AUGCCAUCUAUUCCAAACCCU	97	396-416	AGGGTUTGGAATAGAUGGCAUUU	1578	394-416
AD-1947996	AUGCCAUCUAUUCCAAACCCU	98	396-416	AGGGTUTGGAAUAGAUGGCAUUU	1579	394-416
AD-1947997	UGCCAUCUAUUCCAAACCCUU	99	397-417	AAGGGUTUGGAAUAGAUGGCAUU	1580	395-417
AD-1947998	UGCCAUCUAUUCCAAACCCUU	100	397-417	AAGGGUTUGGAAUAGAUGGCAUU	1581	395-417
AD-1947999	GCCAUCUAUUCCAAACCCUUU	101	398-418	AAAGGGTUUGGAAUAGAUGGCAU	1582	396-418
AD-1948000	GCCAUCUAUUCCAAACCCUUU	102	398-418	AAAGGGTUUGGAAUAGAUGGCAU	1583	396-418
AD-1948001	CCAUCUAUUCCAAACCCUUUU	103	399-419	AAAAGGGUUUGGAAUAGAUGGCA	1584	397-419
AD-1948002	CAUCUAUUCCAAACCCUUUUU	104	400-420	AAAAAGGGUUUGGAAUAGAUGGC	1585	398-420
AD-1948003	AUCUAUUCCAAACCCUUUUCU	105	401-421	AGAAAAGGGUUTGGAAUAGAUGG	1586	399-421
AD-1948004	UCUAUUCCAAACCCUUUUCCU	106	402-422	AGGAAAAGGGUTUGGAAUAGAUG	1587	400-422
AD-1948005	CUAUUCCAAACCCUUUUCCUU	107	403-423	AAGGAAAAGGGTUUGGAAUAGAU	1588	401-423
AD-1948006	UAUUCCAAACCCUUUUCCUGU	108	404-424	ACAGGAAAAGGGUUUGGAAUAGA	1589	402-424
AD-1948007	AUUCCAAACCCUUUUCCUGAU	109	405-425	ATCAGGAAAAGGGUUUGGAAUAG	1590	403-425
AD-1948008	AUUCCAAACCCUUUUCCUGAU	110	405-425	AUCAGGAAAAGGGUUUGGAAUAG	1591	403-425

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948009	UUCCAAACCCUUUUCCUGAGU	111	406-426	ACUCAGGAAAAGGGUUUGGAAUA	1592	404-426
AD-1948010	UCCAAACCCUUUUCCUGAGCU	112	407-427	AGCUCAGGAAAAGGGUUUGGAAU	1593	405-427
AD-1948011	CCAAACCCUUUUCCUGAGCUU	113	408-428	AAGCUCAGGAAAAGGGUUUGGAA	1594	406-428
AD-1948012	CCAAACCCUUUUCCUGAGCUU	114	408-428	AAGCUCAGGAAAAGGGUUUGGAA	1595	406-428
AD-1948013	CAAACCCUUUUCCUGAGCUAU	115	409-429	ATAGCUCAGGAAAAGGGUUUGGA	1596	407-429
AD-1948014	AAACCCUUUUCCUGAGCUAUU	116	410-430	AAUAGCUCAGGAAAAGGGUUUGG	1597	408-430
AD-1948015	AAACCCUUUUCCUGAGCUAUU	117	410-430	AAUAGCUCAGGAAAAGGGUUUGG	1598	408-430
AD-1948016	AACCCUUUUCCUGAGCUAUGU	118	411-431	ACAUAGCUCAGGAAAAGGGUUUG	1599	409-431
AD-1948017	CCCUUUUCCUGAGCUAUGCUU	119	413-433	AAGCAUAGCUCAGGAAAAGGGUU	1600	411-433
AD-1948018	CCUUUUCCUGAGCUAUGCUGU	120	414-434	ACAGCATAGCUCAGGAAAAGGGU	1601	412-434
AD-1948019	CUUUUCCUGAGCUAUGCUGUU	121	415-435	AACAGCAUAGCTCAGGAAAAGGG	1602	413-435
AD-1948020	CUUUUCCUGAGCUAUGCUGUU	122	415-435	AACAGCAUAGCUCAGGAAAAGGG	1603	413-435
AD-1948021	UUUUCCUGAGCUAUGCUGUUU	123	416-436	AAACAGCAUAGCUCAGGAAAAGG	1604	414-436
AD-1948022	UUUCCUGAGCUAUGCUGUUCU	124	417-437	AGAACAGCAUAGCUCAGGAAAAG	1605	415-437
AD-1948023	UUCCUGAGCUAUGCUGUUCUU	125	418-438	AAGAACAGCAUAGCUCAGGAAAA	1606	416-438
AD-1948024	UUCCUGAGCUAUGCUGUUCUU	126	418-438	AAGAACAGCAUAGCUCAGGAAAA	1607	416-438
AD-1948025	CCUGAGCUAUGCUGUUCUCCU	127	420-440	AGGAGAACAGCAUAGCUCAGGAA	1608	418-440
AD-1948026	CCUGAGCUAUGCUGUUCUCCU	128	420-440	AGGAGAACAGCAUAGCUCAGGAA	1609	418-440
AD-1948027	CUGAGCUAUGCUGUUCUCCAU	129	421-441	ATGGAGAACAGCAUAGCUCAGGA	1610	419-441
AD-1948028	CUGAGCUAUGCUGUUCUCCAU	130	421-441	AUGGAGAACAGCAUAGCUCAGGA	1611	419-441
AD-1948029	AUUUACAUCUGUGUUGUCAGU	131	440-460	ACUGACAACACAGAUGUAAAUGG	1612	438-460
AD-1948030	UUUACAUCUGUGUUGUCAGCU	132	441-461	AGCUGACAACACAGAUGUAAAUG	1613	439-461
AD-1948031	UUACAUCUGUGUUGUCAGCAU	133	442-462	ATGCTGACAACACAGAUGUAAAU	1614	440-462
AD-1948032	UUACAUCUGUGUUGUCAGCAU	134	442-462	AUGCTGACAACACAGAUGUAAAU	1615	440-462

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948033	UACAUCUGUGUU GUCAGCAGU	135	443-463	ACUGCUGACAAC ACAGAUGUAAA	1616	441-463
AD-1948034	ACAUCUGUGUUG UCAGCAGAU	136	444-464	ATCUGCTGACAAC ACAGAUGUAA	1617	442-464
AD-1948035	ACAUCUGUGUUG UCAGCAGAU	137	444-464	AUCUGCTGACAAC ACAGAUGUAA	1618	442-464
AD-1948036	UAUUUCCCAAAG CAAAUUCAU	138	466-486	ATGAAUTUGCUTU GGGAAAUAGG	1619	464-486
AD-1948037	UAUUUCCCAAAG CAAAUUCAU	139	466-486	AUGAAUTUGCUU UGGGAAAUAGG	1620	464-486
AD-1948038	AUUUCCCAAAGC AAAUUCAAU	140	467-487	ATUGAATUUGCTU UGGGAAAUAG	1621	465-487
AD-1948039	UUUCCCAAAGCA AAUUCAAGU	141	468-488	ACUUGAAUUUGC UUUGGGAAAUA	1622	466-488
AD-1948040	UUCCCAAAGCAA AUUCAAGGU	142	469-489	ACCUTGAAUUUG CUUUGGGAAAU	1623	467-489
AD-1948041	UCCCAAAGCAAA UUCAAGGAU	143	470-490	ATCCTUGAAUUTG CUUUGGGAAA	1624	468-490
AD-1948042	CCCAAAGCAAAU UCAAGGAAU	144	471-491	ATUCCUTGAAUTU GCUUUGGGAA	1625	469-491
AD-1948043	CCCAAAGCAAAU UCAAGGAAU	145	471-491	AUUCCUTGAAUU UGCUUUGGGAA	1626	469-491
AD-1948044	CCAAAGCAAAUU CAAGGAAAU	146	472-492	ATUUCCTUGAATU UGCUUUGGGA	1627	470-492
AD-1948045	CCAAAGCAAAUU CAAGGAAAU	147	472-492	AUUUCCTUGAAU UUGCUUUGGGA	1628	470-492
AD-1948046	CAAAGCAAAUUC AAGGAAAAU	148	473-493	ATUUTCCUUGAAU UUGCUUUGGG	1629	471-493
AD-1948047	AAAGCAAAUUCA AGGAAAAAU	149	474-494	ATUUTUCCUUGAA UUUGCUUUGG	1630	472-494
AD-1948048	AAGCAAAUUCAA GGAAAAAAU	150	475-495	ATUUTUTCCUUGA AUUUGCUUUG	1631	473-495
AD-1948049	AAGCAAAUUCAA GGAAAAAAU	151	475-495	AUUUTUTCCUUGA AUUUGCUUUG	1632	473-495
AD-1948050	AGCAAAUUCAAG GAAAAAACU	152	476-496	AGUUTUTUCCUTG AAUUUGCUUU	1633	474-496
AD-1948051	AGCAAAUUCAAG GAAAAAACU	153	476-496	AGUUTUTUCCUUG AAUUUGCUUU	1634	474-496
AD-1948052	GCAAAUUCAAGG AAAAAACAU	154	477-497	ATGUTUTUUCCTU GAAUUUGCUU	1635	475-497
AD-1948053	GCAAAUUCAAGG AAAAAACAU	155	477-497	AUGUTUTUUCCUU GAAUUUGCUU	1636	475-497
AD-1948054	CAAAUUCAAGGA AAAAACAGU	156	478-498	ACUGTUTUUUCCU UGAAUUUGCU	1637	476-498
AD-1948055	AAAUUCAAGGAA AAAACAGGU	157	479-499	ACCUGUTUUUUCC UUGAAUUUGC	1638	477-499
AD-1948056	AAUUCAAGGAAA AAACAGGUU	158	480-500	AACCTGTUUUUTC CUUGAAUUUG	1639	478-500

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948057	AAUUCAAGGAAAAAACAGGUU	159	480-500	AACCTGTUUUUUCCUUGAAUUUG	1640	478-500
AD-1948058	AUUCAAGGAAAAAACAGGUGU	160	481-501	ACACCUGUUUUTUCCUUGAAUUU	1641	479-501
AD-1948059	UUCAAGGAAAAAACAGGUGAU	161	482-502	ATCACCTGUUUTUUCCUUGAAUU	1642	480-502
AD-1948060	UUCAAGGAAAAAACAGGUGAU	162	482-502	AUCACCTGUUUUUUCCUUGAAUU	1643	480-502
AD-1948061	UCAAGGAAAAAACAGGUGAUU	163	483-503	AAUCACCUGUUTUUUCCUUGAAU	1644	481-503
AD-1948062	CAAGGAAAAAACAGGUGAUUU	164	484-504	AAAUCACCUGUTUUUUCCUUGAA	1645	482-504
AD-1948063	AAGGAAAAAACAGGUGAUUAU	165	485-505	ATAATCACCUGTUUUUCCUUGA	1646	483-505
AD-1948064	AAGGAAAAAACAGGUGAUUAU	166	485-505	AUAATCACCUGUUUUUCCUUGA	1647	483-505
AD-1948065	AGGAAAAAACAGGUGAUUAAU	167	486-506	ATUAAUCACCUGUUUUUUCCUUG	1648	484-506
AD-1948066	GGAAAAAACAGGUGAUUAAAU	168	487-507	ATUUAATCACCTGUUUUUUCCUU	1649	485-507
AD-1948067	GGAAAAAACAGGUGAUUAAAU	169	487-507	AUUUAATCACCUGUUUUUUCCUU	1650	485-507
AD-1948068	GAAAAAACAGGUGAUUAAAGU	170	488-508	ACUUTAAUCACCUGUUUUUUCCU	1651	486-508
AD-1948069	AAAAAACAGGUGAUUAAAGUU	171	489-509	AACUTUAAUCACCUGUUUUUUCC	1652	487-509
AD-1948070	UAUACAGUGAAGAUGAAACCU	172	508-528	AGGUTUCAUCUTCACUGUAUACU	1653	506-528
AD-1948071	AUACAGUGAAGAUGAAACCAU	173	509-529	ATGGTUTCAUCTUCACUGUAUAC	1654	507-529
AD-1948072	AUACAGUGAAGAUGAAACCAU	174	509-529	AUGGTUTCAUCUUCACUGUAUAC	1655	507-529
AD-1948073	UACAGUGAAGAUGAAACCAGU	175	510-530	ACUGGUTUCAUCUUCACUGUAUA	1656	508-530
AD-1948074	GCAGGGCUUUAGAUGUACCCU	176	529-549	AGGGTACAUCUAAAGCCCUGCUG	1657	527-549
AD-1948075	CAGGGCUUUAGAUGUACCCAU	177	530-550	ATGGGUACAUCTAAAGCCCUGCU	1658	528-550
AD-1948076	CAGGGCUUUAGAUGUACCCAU	178	530-550	AUGGGUACAUCUAAAGCCCUGCU	1659	528-550
AD-1948077	AGGGCUUUAGAUGUACCCAGU	179	531-551	ACUGGGTACAUCUAAAGCCCUGC	1660	529-551
AD-1948078	AGGGCUUUAGAUGUACCCAGU	180	531-551	ACUGGGTACAUCUAAAGCCCUGC	1661	529-551
AD-1948079	GGGCUUUAGAUGUACCCAGUU	181	532-552	AACUGGGUACATCUAAAGCCCUG	1662	530-552
AD-1948080	GGCUUUAGAUGUACCCAGUGU	182	533-553	ACACTGGGUACAUCUAAAGCCCU	1663	531-553

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948081	GCUUUAGAUGUACCCAGUGAU	183	534-554	ATCACUGGGUACAUCUAAAGCCC	1664	532-554
AD-1948082	UUUAGAUGUACCCAGUGACAU	184	536-556	ATGUCACUGGGTACAUCUAAAGC	1665	534-556
AD-1948083	UUAGAUGUACCCAGUGACAUU	185	537-557	AAUGTCACUGGGUACAUCUAAAG	1666	535-557
AD-1948084	UUAGAUGUACCCAGUGACAUU	186	537-557	AAUGTCACUGGGUACAUCUAAAG	1667	535-557
AD-1948085	UAGAUGUACCCAGUGACAUAU	187	538-558	ATAUGUCACUGGGUACAUCUAAA	1668	536-558
AD-1948086	AGAUGUACCCAGUGACAUAAU	188	539-559	ATUATGTCACUGGGUACAUCUAA	1669	537-559
AD-1948087	AGAUGUACCCAGUGACAUAAU	189	539-559	AUUATGTCACUGGGUACAUCUAA	1670	537-559
AD-1948088	GAUGUACCCAGUGACAUAACU	190	540-560	AGUUAUGUCACTGGGUACAUCUA	1671	538-560
AD-1948089	UGUACCCAGUGACAUAACGGU	191	542-562	ACCGTUAUGUCACUGGGUACAUC	1672	540-562
AD-1948090	GUACCCAGUGACAUAACGGCU	192	543-563	AGCCGUTAUGUCACUGGGUACAU	1673	541-563
AD-1948091	UACCCAGUGACAUAACGGCUU	193	544-564	AAGCCGTUAUGTCACUGGGUACA	1674	542-564
AD-1948092	ACCCAGUGACAUAACGGCUCU	194	545-565	AGAGCCGUUAUGUCACUGGGUAC	1675	543-565
AD-1948093	CCAGUGACAUAACGGCUCGAU	195	547-567	ATCGAGCCGUUAUGUCACUGGGU	1676	545-567
AD-1948094	CAGUGACAUAACGGCUCGAGU	196	548-568	ACUCGAGCCGUTAUGUCACUGGG	1677	546-568
AD-1948095	GUGACAUAACGGCUCGAGAUU	197	550-570	AAUCTCGAGCCGUUAUGUCACUG	1678	548-570
AD-1948096	UGACAUAACGGCUCGAGAUGU	198	551-571	ACAUCUCGAGCCGUUAUGUCACU	1679	549-571
AD-1948097	GACAUAACGGCUCGAGAUGUU	199	552-572	AACATCTCGAGCCGUUAUGUCAC	1680	550-572
AD-1948098	GACAUAACGGCUCGAGAUGUU	200	552-572	AACATCTCGAGCCGUUAUGUCAC	1681	550-572
AD-1948099	ACAUAACGGCUCGAGAUGUUU	201	553-573	AAACAUCUCGAGCCGUUAUGUCA	1682	551-573
AD-1948100	CAUAACGGCUCGAGAUGUUUU	202	554-574	AAAACATCUCGAGCCGUUAUGUC	1683	552-574
AD-1948101	CAUAACGGCUCGAGAUGUUUU	203	554-574	AAAACATCUCGAGCCGUUAUGUC	1684	552-574
AD-1948102	AUAACGGCUCGAGAUGUUUGU	204	555-575	ACAAACAUCUCGAGCCGUUAUGU	1685	553-575
AD-1948103	UAACGGCUCGAGAUGUUUGUU	205	556-576	AACAAACAUCUCGAGCCGUUAUG	1686	554-576
AD-1948104	AACGGCUCGAGAUGUUUGUCU	206	557-577	AGACAAACAUCTCGAGCCGUUAU	1687	555-577

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948105	ACGGCUCGAGAU GUUUGUCAU	207	558-578	ATGACAAACAUC UCGAGCCGUUA	1688	556-578
AD-1948106	CGGCUCGAGAUG UUUGUCAGU	208	559-579	ACUGACAAACATC UCGAGCCGUU	1689	557-579
AD-1948107	GGCUCGAGAUGU UUGUCAGCU	209	560-580	AGCUGACAAACA UCUCGAGCCGU	1690	558-580
AD-1948108	GCUCGAGAUGUU UGUCAGCUU	210	561-581	AAGCTGACAAAC AUCUCGAGCCG	1691	559-581
AD-1948109	GCUCGAGAUGUU UGUCAGCUU	211	561-581	AAGCTGACAAAC AUCUCGAGCCG	1692	559-581
AD-1948110	CUCGAGAUGUUU GUCAGCUGU	212	562-582	ACAGCUGACAAA CAUCUCGAGCC	1693	560-582
AD-1948111	UCGAGAUGUUUG UCAGCUGUU	213	563-583	AACAGCTGACAA ACAUCUCGAGC	1694	561-583
AD-1948112	UCGAGAUGUUUG UCAGCUGUU	214	563-583	AACAGCTGACAA ACAUCUCGAGC	1695	561-583
AD-1948113	CGAGAUGUUUGU CAGCUGUUU	215	564-584	AAACAGCUGACA AACAUCUCGAG	1696	562-584
AD-1948114	GAGAUGUUUGUC AGCUGUUGU	216	565-585	ACAACAGCUGAC AAACAUCUCGA	1697	563-585
AD-1948115	AGAUGUUUGUCA GCUGUUGAU	217	566-586	ATCAACAGCUGAC AAACAUCUCG	1698	564-586
AD-1948116	AGAUGUUUGUCA GCUGUUGAU	218	566-586	AUCAACAGCUGA CAAACAUCUCG	1699	564-586
AD-1948117	GAUGUUUGUCAG CUGUUGAUU	219	567-587	AAUCAACAGCUG ACAAACAUCUC	1700	565-587
AD-1948118	AUGUUUGUCAGC UGUUGAUCU	220	568-588	AGAUCAACAGCT GACAAACAUCU	1701	566-588
AD-1948119	AUGUUUGUCAGC UGUUGAUCU	221	568-588	AGAUCAACAGCU GACAAACAUCU	1702	566-588
AD-1948120	UGUUUGUCAGCU GUUGAUCCU	222	569-589	AGGATCAACAGC UGACAAACAUC	1703	567-589
AD-1948121	UGUUUGUCAGCU GUUGAUCCU	223	569-589	AGGATCAACAGC UGACAAACAUC	1704	567-589
AD-1948122	GUUUGUCAGCUG UUGAUCCUU	224	570-590	AAGGAUCAACAG CUGACAAACAU	1705	568-590
AD-1948123	UUUGUCAGCUGU UGAUCCUGU	225	571-591	ACAGGATCAACA GCUGACAAACA	1706	569-591
AD-1948124	UUGUCAGCUGUU GAUCCUGAU	226	572-592	ATCAGGAUCAAC AGCUGACAAAC	1707	570-592
AD-1948125	UUGUCAGCUGUU GAUCCUGAU	227	572-592	AUCAGGAUCAAC AGCUGACAAAC	1708	570-592
AD-1948126	UGUCAGCUGUUG AUCCUGAAU	228	573-593	ATUCAGGAUCAA CAGCUGACAAA	1709	571-593
AD-1948127	GUCAGCUGUUGA UCCUGAAGU	229	574-594	ACUUCAGGAUCA ACAGCUGACAA	1710	572-594
AD-1948128	UCAGCUGUUGAU CCUGAAGAU	230	575-595	ATCUTCAGGAUCA ACAGCUGACA	1711	573-595

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948129	UCAGCUGUUGAUCCUGAAGAU	231	575-595	AUCUTCAGGAUCAACAGCUGACA	1712	573-595
AD-1948130	CAGCUGUUGAUCCUGAAGAAU	232	576-596	ATUCTUCAGGATCAACAGCUGAC	1713	574-596
AD-1948131	AGCUGUUGAUCCUGAAGAAUU	233	577-597	AAUUCUTCAGGAUCAACAGCUGA	1714	575-597
AD-1948132	AGCUGUUGAUCCUGAAGAAUU	234	577-597	AAUUCUTCAGGAUCAACAGCUGA	1715	575-597
AD-1948133	GCUGUUGAUCCUGAAGAAUCU	235	578-598	AGAUTCTUCAGGAUCAACAGCUG	1716	576-598
AD-1948134	GCUGUUGAUCCUGAAGAAUCU	236	578-598	AGAUTCTUCAGGAUCAACAGCUG	1717	576-598
AD-1948135	CUGUUGAUCCUGAAGAAUCAU	237	579-599	ATGATUCUUCAGGAUCAACAGCU	1718	577-599
AD-1948136	UGUUGAUCCUGAAGAAUCAUU	238	580-600	AAUGAUTCUUCAGGAUCAACAGC	1719	578-600
AD-1948137	GUUGAUCCUGAAGAAUCAUUU	239	581-601	AAAUGATUCUUCAGGAUCAACAG	1720	579-601
AD-1948138	GUUGAUCCUGAAGAAUCAUUU	240	581-601	AAAUGATUCUUCAGGAUCAACAG	1721	579-601
AD-1948139	UUGAUCCUGAAGAAUCAUUAU	241	582-602	ATAATGAUUCUTCAGGAUCAACA	1722	580-602
AD-1948140	UUGAUCCUGAAGAAUCAUUAU	242	582-602	AUAATGAUUCUUCAGGAUCAACA	1723	580-602
AD-1948141	UGAUCCUGAAGAAUCAUUACU	243	583-603	AGUAAUGAUUCTUCAGGAUCAAC	1724	581-603
AD-1948142	GAUCCUGAAGAAUCAUUACAU	244	584-604	ATGUAATGAUUCUUCAGGAUCAA	1725	582-604
AD-1948143	CCCUUUUUGAGCACCUGCCUU	245	622-642	AAGGCAGGUGCTCAAAAAGGGUC	1726	620-642
AD-1948144	CCUUUUUGAGCACCUGCCUCU	246	623-643	AGAGGCAGGUGCUCAAAAAGGGU	1727	621-643
AD-1948145	CCUUUUUGAGCACCUGCCUCU	247	623-643	AGAGGCAGGUGCUCAAAAAGGGU	1728	621-643
AD-1948146	CUUUUUGAGCACCUGCCUCAU	248	624-644	ATGAGGCAGGUGCUCAAAAAGGG	1729	622-644
AD-1948147	GAGCACCUGCCUCACAUAGGU	249	630-650	ACCUAUGUGAGGCAGGUGCUCAA	1730	628-650
AD-1948148	CACCUGCCUCACAUAGGUGUU	250	633-653	AACACCTAUGUGAGGCAGGUGCU	1731	631-653
AD-1948149	GCCUCACAUAGGUGUAGAAAU	251	638-658	ATUUCUACACCTAUGUGAGGCAG	1732	636-658
AD-1948150	GCCUCACAUAGGUGUAGAAAU	252	638-658	AUUUCUACACCUAUGUGAGGCAG	1733	636-658
AD-1948151	CCUCACAUAGGUGUAGAAAGU	253	639-659	ACUUTCTACACCUAUGUGAGGCA	1734	637-659
AD-1948152	CCUCACAUAGGUGUAGAAAGU	254	639-659	ACUUTCTACACCUAUGUGAGGCA	1735	637-659

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948153	CUCACAUAGGUG UAGAAAGAU	255	640-660	ATCUTUCUACACC UAUGUGAGGC	1736	638-660
AD-1948154	UCACAUAGGUGU AGAAAGAAU	256	641-661	ATUCTUTCUACAC CUAUGUGAGG	1737	639-661
AD-1948155	UCACAUAGGUGU AGAAAGAAU	257	641-661	AUUCTUTCUACAC CUAUGUGAGG	1738	639-661
AD-1948156	CACAUAGGUGUA GAAAGAACU	258	642-662	AGUUCUTUCUAC ACCUAUGUGAG	1739	640-662
AD-1948157	CACAUAGGUGUA GAAAGAACU	259	642-662	AGUUCUTUCUAC ACCUAUGUGAG	1740	640-662
AD-1948158	ACAUAGGUGUAG AAAGAACAU	260	643-663	ATGUTCTUUCUAC ACCUAUGUGA	1741	641-663
AD-1948159	ACAUAGGUGUAG AAAGAACAU	261	643-663	AUGUTCTUUCUAC ACCUAUGUGA	1742	641-663
AD-1948160	CAUAGGUGUAGA AAGAACAAU	262	644-664	ATUGTUCUUUCTA CACCUAUGUG	1743	642-664
AD-1948161	AUAGGUGUAGA AAGAACAAUU	263	645-665	AAUUGUTCUUUC UACACCUAUGU	1744	643-665
AD-1948162	AUAGGUGUAGA AAGAACAAUU	264	645-665	AAUUGUTCUUUC UACACCUAUGU	1745	643-665
AD-1948163	UAGGUGUAGAA AGAACAAUAU	265	646-666	ATAUTGTUCUUTC UACACCUAUG	1746	644-666
AD-1948164	UAGGUGUAGAA AGAACAAUAU	266	646-666	AUAUTGTUCUUUC UACACCUAUG	1747	644-666
AD-1948165	AGGUGUAGAAA GAACAAUAGU	267	647-667	ACUATUGUUCUTU CUACACCUAU	1748	645-667
AD-1948166	GGUGUAGAAAG AACAAUAGAU	268	648-668	ATCUAUTGUUCTU UCUACACCUA	1749	646-668
AD-1948167	GUGUAGAAAGA ACAAUAGAAU	269	649-669	ATUCTATUGUUCU UUCUACACCU	1750	647-669
AD-1948168	GUGUAGAAAGA ACAAUAGAAU	270	649-669	AUUCTATUGUUCU UUCUACACCU	1751	647-669
AD-1948169	UGUAGAAAGAAC AAUAGAAGU	271	650-670	ACUUCUAUUGUT CUUUCUACACC	1752	648-670
AD-1948170	GUAGAAAGAACA AUAGAAGAU	272	651-671	ATCUTCTAUUGTU CUUUCUACAC	1753	649-671
AD-1948171	GUAGAAAGAACA AUAGAAGAU	273	651-671	AUCUTCTAUUGUU CUUUCUACAC	1754	649-671
AD-1948172	UAGAAAGAACAA UAGAAGACU	274	652-672	AGUCTUCUAUUG UUCUUUCUACA	1755	650-672
AD-1948173	AGAAAGAACAAU AGAAGACCU	275	653-673	AGGUCUTCUAUTG UUCUUUCUAC	1756	651-673
AD-1948174	AGAAAGAACAAU AGAAGACCU	276	653-673	AGGUCUTCUAUU GUUCUUUCUAC	1757	651-673
AD-1948175	GAAAGAACAAUA GAAGACCAU	277	654-674	ATGGTCTUCUATU GUUCUUUCUA	1758	652-674
AD-1948176	GAAAGAACAAUA GAAGACCAU	278	654-674	AUGGTCTUCUAUU GUUCUUUCUA	1759	652-674

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948177	ACGAACUGGUGA UUGAAGUGU	279	673-693	ACACTUCAAUCAC CAGUUCGUGG	1760	671-693
AD-1948178	CGAACUGGUGAU UGAAGUGCU	280	674-694	AGCACUTCAAUCA CCAGUUCGUG	1761	672-694
AD-1948179	CGAACUGGUGAU UGAAGUGCU	281	674-694	AGCACUTCAAUCA CCAGUUCGUG	1762	672-694
AD-1948180	GAACUGGUGAUU GAAGUGCUU	282	675-695	AAGCACTUCAATC ACCAGUUCGU	1763	673-695
AD-1948181	GAACUGGUGAUU GAAGUGCUU	283	675-695	AAGCACTUCAAUC ACCAGUUCGU	1764	673-695
AD-1948182	AACUGGUGAUUG AAGUGCUAU	284	676-696	ATAGCACUUCAA UCACCAGUUCG	1765	674-696
AD-1948183	ACUGGUGAUUGA AGUGCUAUU	285	677-697	AAUAGCACUUCA AUCACCAGUUC	1766	675-697
AD-1948184	ACUGGUGAUUGA AGUGCUAUU	286	677-697	AAUAGCACUUCA AUCACCAGUUC	1767	675-697
AD-1948185	CUGGUGAUUGAA GUGCUAUCU	287	678-698	AGAUAGCACUUC AAUCACCAGUU	1768	676-698
AD-1948186	UGGUGAUUGAA GUGCUAUCCU	288	679-699	AGGATAGCACUTC AAUCACCAGU	1769	677-699
AD-1948187	GGUGAUUGAAG UGCUAUCCAU	289	680-700	ATGGAUAGCACTU CAAUCACCAG	1770	678-700
AD-1948188	GGUGAUUGAAG UGCUAUCCAU	290	680-700	AUGGAUAGCACU UCAAUCACCAG	1771	678-700
AD-1948189	GUGAUUGAAGU GCUAUCCAAU	291	681-701	ATUGGATAGCACU UCAAUCACCA	1772	679-701
AD-1948190	GUGAUUGAAGU GCUAUCCAAU	292	681-701	AUUGGATAGCAC UUCAAUCACCA	1773	679-701
AD-1948191	UGAUUGAAGUGC UAUCCAACU	293	682-702	AGUUGGAUAGCA CUUCAAUCACC	1774	680-702
AD-1948192	UGAUUGAAGUGC UAUCCAACU	294	682-702	AGUUGGAUAGCA CUUCAAUCACC	1775	680-702
AD-1948193	GAUUGAAGUGCU AUCCAACUU	295	683-703	AAGUTGGAUAGC ACUUCAAUCAC	1776	681-703
AD-1948194	AUUGAAGUGCUA UCCAACUGU	296	684-704	ACAGTUGGAUAG CACUUCAAUCA	1777	682-704
AD-1948195	UUGAAGUGCUAU CCAACUGGU	297	685-705	ACCAGUTGGAUA GCACUUCAAUC	1778	683-705
AD-1948196	AAAAAUUAUGCC AAAUAUGAU	298	738-758	ATCATATUUGGCA UAAUUUUUUC	1779	736-758
AD-1948197	AAUUAUGCCAAA UAUGAGUUU	299	741-761	AAACTCAUAUUTG GCAUAAUUUU	1780	739-761
AD-1948198	AAUUAUGCCAAA UAUGAGUUU	300	741-761	AAACTCAUAUUU GGCAUAAUUUU	1781	739-761
AD-1948199	AUUAUGCCAAAU AUGAGUUCU	301	742-762	AGAACUCAUAUT UGGCAUAAUUU	1782	740-762
AD-1948200	UUAUGCCAAAUA UGAGUUCUU	302	743-763	AAGAACTCAUATU UGGCAUAAUU	1783	741-763

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948201	UUAUGCCAAAUAUGAGUUCUU	303	743-763	AAGAACTCAUAUUUGGCAUAAUU	1784	741-763
AD-1948202	UAUGCCAAAUAUGAGUUCUUU	304	744-764	AAAGAACUCAUAUUUGGCAUAAU	1785	742-764
AD-1948203	AUGCCAAAUAUGAGUUCUUUU	305	745-765	AAAAGAACUCATAUUUGGCAUAA	1786	743-765
AD-1948204	AUGCCAAAUAUGAGUUCUUUU	306	745-765	AAAAGAACUCAUAUUUGGCAUAA	1787	743-765
AD-1948205	UGCCAAAUAUGAGUUCUUUAU	307	746-766	ATAAAGAACUCAUAUUUGGCAUA	1788	744-766
AD-1948206	GCCAAAUAUGAGUUCUUUAAU	308	747-767	ATUAAAGAACUCAUAUUUGGCAU	1789	745-767
AD-1948207	CCAAAUAUGAGUUCUUUAAAU	309	748-768	ATUUAAAGAACTCAUAUUUGGCA	1790	746-768
AD-1948208	CAAAUAUGAGUUCUUUAAAAU	310	749-769	ATUUTAAAGAACUCAUAUUUGGC	1791	747-769
AD-1948209	AAAUAUGAGUUCUUUAAAAAU	311	750-770	ATUUTUAAAGAACUCAUAUUUGG	1792	748-770
AD-1948210	AAUAUGAGUUCUUUAAAAACU	312	751-771	AGUUTUTAAAGAACUCAUAUUUG	1793	749-771
AD-1948211	AAUAUGAGUUCUUUAAAAACU	313	751-771	AGUUTUTAAAGAACUCAUAUUUG	1794	749-771
AD-1948212	AUAUGAGUUCUUUAAAAACCU	314	752-772	AGGUTUTUAAAGAACUCAUAUUU	1795	750-772
AD-1948213	AUAUGAGUUCUUUAAAAACCU	315	752-772	AGGUTUTUAAAGAACUCAUAUUU	1796	750-772
AD-1948214	UAUGAGUUCUUUAAAAACCCU	316	753-773	AGGGTUTUUAAAGAACUCAUAUU	1797	751-773
AD-1948215	UAUGAGUUCUUUAAAAACCCU	317	753-773	AGGGTUTUUAAAGAACUCAUAUU	1798	751-773
AD-1948216	AUGAGUUCUUUAAAAACCCAU	318	754-774	ATGGGUTUUUAAAGAACUCAUAU	1799	752-774
AD-1948217	AUGAGUUCUUUAAAAACCCAU	319	754-774	AUGGGUTUUUAAAGAACUCAUAU	1800	752-774
AD-1948218	UGAGUUCUUUAAAAACCCAAU	320	755-775	ATUGGGTUUUUAAAGAACUCAUA	1801	753-775
AD-1948219	UGAGUUCUUUAAAAACCCAAU	321	755-775	AUUGGGTUUUUAAAGAACUCAUA	1802	753-775
AD-1948220	GAGUUCUUUAAAAACCCAAUU	322	756-776	AAUUGGGUUUUTAAAGAACUCAU	1803	754-776
AD-1948221	AGUUCUUUAAAAACCCAAUGU	323	757-777	ACAUTGGGUUUTUAAAGAACUCA	1804	755-777
AD-1948222	GUUCUUUAAAAACCCAAUGUU	324	758-778	AACATUGGGUUTUUAAAGAACUC	1805	756-778
AD-1948223	UUCUUUAAAAACCCAAUGUAU	325	759-779	ATACAUTGGGUTUUUAAAGAACU	1806	757-779
AD-1948224	UCUUUAAAAACCCAAUGUAUU	326	760-780	AAUACATUGGGTUUUUAAAGAAC	1807	758-780

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948225	AAACCCAAUGUAUUUUUUUCU	327	767-787	AGAAAAAAAUACAUUGGGUUUUU	1808	765-787
AD-1948226	AACCCAAUGUAUUUUUUUCCU	328	768-788	AGGAAAAAAAUACAUUGGGUUUU	1809	766-788
AD-1948227	ACCCAAUGUAUUUUUUUCCAU	329	769-789	ATGGAAAAAAATACAUUGGGUUU	1810	767-789
AD-1948228	CCCAAUGUAUUUUUUUCCAGU	330	770-790	ACUGGAAAAAAAUACAUUGGGUU	1811	768-790
AD-1948229	CCAAUGUAUUUUUUUCCAGAU	331	771-791	ATCUGGAAAAAAAUACAUUGGGU	1812	769-791
AD-1948230	CCAAUGUAUUUUUUUCCAGAU	332	771-791	AUCUGGAAAAAAAUACAUUGGGU	1813	769-791
AD-1948231	CAAUGUAUUUUUUUCCAGAGU	333	772-792	ACUCTGGAAAAAAAUACAUUGGG	1814	770-792
AD-1948232	AAUGUAUUUUUUUCCAGAGCU	334	773-793	AGCUCUGGAAAAAAAUACAUUGG	1815	771-793
AD-1948233	AUGUAUUUUUUUCCAGAGCAU	335	774-794	ATGCTCTGGAAAAAAAUACAUUG	1816	772-794
AD-1948234	AUGUAUUUUUUUCCAGAGCAU	336	774-794	AUGCTCTGGAAAAAAAUACAUUG	1817	772-794
AD-1948235	UGUAUUUUUUUCCAGAGCAUU	337	775-795	AAUGCUCUGGAAAAAAAUACAUU	1818	773-795
AD-1948236	GUAUUUUUUUCCAGAGCAUAU	338	776-796	ATAUGCTCUGGAAAAAAAUACAU	1819	774-796
AD-1948237	GUAUUUUUUUCCAGAGCAUAU	339	776-796	AUAUGCTCUGGAAAAAAAUACAU	1820	774-796
AD-1948238	UAUUUUUUUCCAGAGCAUAUU	340	777-797	AAUATGCUCUGGAAAAAAAUACA	1821	775-797
AD-1948239	AUUUUUUUCCAGAGCAUAUGU	341	778-798	ACAUAUGCUCUGGAAAAAAAUAC	1822	776-798
AD-1948240	UUUUUUUCCAGAGCAUAUGGU	342	779-799	ACCATATGCUCTGGAAAAAAAUA	1823	777-799
AD-1948241	UUUUUUCCAGAGCAUAUGGUU	343	780-800	AACCAUAUGCUCUGGAAAAAAAU	1824	778-800
AD-1948242	UUUUUCCAGAGCAUAUGGUAU	344	781-801	ATACCATAUGCTCUGGAAAAAAA	1825	779-801
AD-1948243	UUUUCCAGAGCAUAUGGUAUU	345	782-802	AAUACCAUAUGCUCUGGAAAAAA	1826	780-802
AD-1948244	UUUUCCAGAGCAUAUGGUAUU	346	782-802	AAUACCAUAUGCUCUGGAAAAAA	1827	780-802
AD-1948245	UUUCCAGAGCAUAUGGUAUCU	347	783-803	AGAUACCAUAUGCUCUGGAAAAA	1828	781-803
AD-1948246	UUCCAGAGCAUAUGGUAUCUU	348	784-804	AAGATACCAUATGCUCUGGAAAA	1829	782-804
AD-1948247	UCCAGAGCAUAUGGUAUCUUU	349	785-805	AAAGAUACCAUAUGCUCUGGAAA	1830	783-805
AD-1948248	CCAGAGCAUAUGGUAUCUUUU	350	786-806	AAAAGATACCATAUGCUCUGGAA	1831	784-806

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948249	CCAGAGCAUAUG GUAUCUUUU	351	786-806	AAAAGATACCAU AUGCUCUGGAA	1832	784-806
AD-1948250	CAGAGCAUAUGG UAUCUUUUU	352	787-807	AAAAAGAUACCA UAUGCUCUGGA	1833	785-807
AD-1948251	CAGAGCAUAUGG UAUCUUUUU	353	787-807	AAAAAGAUACCA UAUGCUCUGGA	1834	785-807
AD-1948252	AGAGCAUAUGGU AUCUUUUGU	354	788-808	ACAAAAGAUACC AUAUGCUCUGG	1835	786-808
AD-1948253	GAGCAUAUGGUA UCUUUUGCU	355	789-809	AGCAAAAGAUAC CAUAUGCUCUG	1836	787-809
AD-1948254	AGCAUAUGGUAU CUUUUGCAU	356	790-810	ATGCAAAAGAUA CCAUAUGCUCU	1837	788-810
AD-1948255	GCAUAUGGUAUC UUUUGCAAU	357	791-811	ATUGCAAAAGAT ACCAUAUGCUC	1838	789-811
AD-1948256	CAUAUGGUAUCU UUUGCAACU	358	792-812	AGUUGCAAAAGA UACCAUAUGCU	1839	790-812
AD-1948257	CAUAUGGUAUCU UUUGCAACU	359	792-812	AGUUGCAAAAGA UACCAUAUGCU	1840	790-812
AD-1948258	AUAUGGUAUCUU UUGCAACUU	360	793-813	AAGUTGCAAAAG AUACCAUAUGC	1841	791-813
AD-1948259	UAUGGUAUCUUU UGCAACUGU	361	794-814	ACAGTUGCAAAA GAUACCAUAUG	1842	792-814
AD-1948260	AUGGUAUCUUUU GCAACUGAU	362	795-815	ATCAGUTGCAAAA GAUACCAUAU	1843	793-815
AD-1948261	AUGGUAUCUUUU GCAACUGAU	363	795-815	AUCAGUTGCAAA AGAUACCAUAU	1844	793-815
AD-1948262	UGGUAUCUUUUG CAACUGAAU	364	796-816	ATUCAGTUGCAAA AGAUACCAUA	1845	794-816
AD-1948263	UGGUAUCUUUUG CAACUGAAU	365	796-816	AUUCAGTUGCAA AAGAUACCAUA	1846	794-816
AD-1948264	GGUAUCUUUUGC AACUGAAAU	366	797-817	ATUUCAGUUGCA AAAGAUACCAU	1847	795-817
AD-1948265	GUAUCUUUUGCA ACUGAAACU	367	798-818	AGUUTCAGUUGC AAAAGAUACCA	1848	796-818
AD-1948266	GUAUCUUUUGCA ACUGAAACU	368	798-818	AGUUTCAGUUGC AAAAGAUACCA	1849	796-818
AD-1948267	UAUCUUUUGCAA CUGAAACCU	369	799-819	AGGUTUCAGUUG CAAAAGAUACC	1850	797-819
AD-1948268	AUCUUUUGCAAC UGAAACCAU	370	800-820	ATGGTUTCAGUTG CAAAAGAUAC	1851	798-820
AD-1948269	AUCUUUUGCAAC UGAAACCAU	371	800-820	AUGGTUTCAGUU GCAAAAGAUAC	1852	798-820
AD-1948270	UCUUUUGCAACU GAAACCAAU	372	801-821	ATUGGUTUCAGTU GCAAAAGAUA	1853	799-821
AD-1948271	UCUUUUGCAACU GAAACCAAU	373	801-821	AUUGGUTUCAGU UGCAAAAGAUA	1854	799-821
AD-1948272	CUUUUGCAACUG AAACCAAUU	374	802-822	AAUUGGTUUCAG UUGCAAAAGAU	1855	800-822

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948273	CUUUUGCAACUG AAACCAAUU	375	802-822	AAUUGGTUUCAG UUGCAAAAGAU	1856	800-822
AD-1948274	UUUUGCAACUGA AACCAAUGU	376	803-823	ACAUTGGUUUCA GUUGCAAAAGA	1857	801-823
AD-1948275	UUGCAGAUGUUU CUGAGUUCU	377	846-866	AGAACUCAGAAA CAUCUGCAAAA	1858	844-866
AD-1948276	UGCAGAUGUUUC UGAGUUCAU	378	847-867	ATGAACTCAGAAA CAUCUGCAAA	1859	845-867
AD-1948277	UGCAGAUGUUUC UGAGUUCAU	379	847-867	AUGAACTCAGAA ACAUCUGCAAA	1860	845-867
AD-1948278	GCAGAUGUUUCU GAGUUCAAU	380	848-868	ATUGAACUCAGA AACAUCUGCAA	1861	846-868
AD-1948279	CAGAUGUUUCUG AGUUCAAGU	381	849-869	ACUUGAACUCAG AAACAUCUGCA	1862	847-869
AD-1948280	CAGAUGUUUCUG AGUUCAAGU	382	849-869	ACUUGAACUCAG AAACAUCUGCA	1863	847-869
AD-1948281	AGAUGUUUCUGA GUUCAAGCU	383	850-870	AGCUTGAACUCA GAAACAUCUGC	1864	848-870
AD-1948282	AGAUGUUUCUGA GUUCAAGCU	384	850-870	AGCUTGAACUCA GAAACAUCUGC	1865	848-870
AD-1948283	GAUGUUUCUGAG UUCAAGCAU	385	851-871	ATGCTUGAACUCA GAAACAUCUG	1866	849-871
AD-1948284	AUGUUUCUGAGU UCAAGCACU	386	852-872	AGUGCUTGAACTC AGAAACAUCU	1867	850-872
AD-1948285	AUGUUUCUGAGU UCAAGCACU	387	852-872	AGUGCUTGAACU CAGAAACAUCU	1868	850-872
AD-1948286	UGUUUCUGAGUU CAAGCACAU	388	853-873	ATGUGCTUGAACU CAGAAACAUC	1869	851-873
AD-1948287	UGUUUCUGAGUU CAAGCACAU	389	853-873	AUGUGCTUGAAC UCAGAAACAUC	1870	851-873
AD-1948288	GUUUCUGAGUUC AAGCACAUU	390	854-874	AAUGTGCUUGAA CUCAGAAACAU	1871	852-874
AD-1948289	UUUCUGAGUUCA AGCACAUAU	391	855-875	ATAUGUGCUUGA ACUCAGAAACA	1872	853-875
AD-1948290	AUCCUGAAAUUC AUGGUUUCU	392	874-894	AGAAACCAUGAA UUUCAGGAUAU	1873	872-894
AD-1948291	UCCUGAAAUUCA UGGUUUCUU	393	875-895	AAGAAACCAUGA AUUUCAGGAUA	1874	873-895
AD-1948292	CCUGAAAUUCAU GGUUUCUUU	394	876-896	AAAGAAACCAUG AAUUUCAGGAU	1875	874-896
AD-1948293	CUGAAAUUCAUG GUUUCUUAU	395	877-897	ATAAGAAACCATG AAUUUCAGGA	1876	875-897
AD-1948294	UGAAAUUCAUGG UUUCUUACU	396	878-898	AGUAAGAAACCA UGAAUUUCAGG	1877	876-898
AD-1948295	UGAAAUUCAUGG UUUCUUACU	397	878-898	AGUAAGAAACCA UGAAUUUCAGG	1878	876-898
AD-1948296	GAAAUUCAUGGU UUCUUACAU	398	879-899	ATGUAAGAAACC AUGAAUUUCAG	1879	877-899

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948297	AAAUUCAUGGUUUCUUACAUU	399	880-900	AAUGTAAGAAACCAUGAAUUUCA	1880	878-900
AD-1948298	AAUUCAUGGUUUCUUACAUGU	400	881-901	ACAUGUAAGAAACCAUGAAUUUC	1881	879-901
AD-1948299	AUUCAUGGUUUCUUACAUGCU	401	882-902	AGCATGTAAGAAACCAUGAAUUU	1882	880-902
AD-1948300	AUUCAUGGUUUCUUACAUGCU	402	882-902	AGCATGTAAGAAACCAUGAAUUU	1883	880-902
AD-1948301	UUCAUGGUUUCUUACAUGCGU	403	883-903	ACGCAUGUAAGAAACCAUGAAUU	1884	881-903
AD-1948302	UCAUGGUUUCUUACAUGCGAU	404	884-904	ATCGCATGUAAGAAACCAUGAAU	1885	882-904
AD-1948303	UCAUGGUUUCUUACAUGCGAU	405	884-904	AUCGCATGUAAGAAACCAUGAAU	1886	882-904
AD-1948304	CAUGGUUUCUUACAUGCGAAU	406	885-905	ATUCGCAUGUAAGAAACCAUGAA	1887	883-905
AD-1948305	CAUGGUUUCUUACAUGCGAAU	407	885-905	AUUCGCAUGUAAGAAACCAUGAA	1888	883-905
AD-1948306	AUGGUUUCUUACAUGCGAAAU	408	886-906	ATUUCGCAUGUAAGAAACCAUGA	1889	884-906
AD-1948307	UGGUUUCUUACAUGCGAAAGU	409	887-907	ACUUTCGCAUGTAAGAAACCAUG	1890	885-907
AD-1948308	GGUUUCUUACAUGCGAAAGAU	410	888-908	ATCUTUCGCAUGUAAGAAACCAU	1891	886-908
AD-1948309	GUUUCUUACAUGCGAAAGAAU	411	889-909	ATUCTUTCGCATGUAAGAAACCA	1892	887-909
AD-1948310	GUUUCUUACAUGCGAAAGAAU	412	889-909	AUUCTUTCGCAUGUAAGAAACCA	1893	887-909
AD-1948311	UUUCUUACAUGCGAAAGAACU	413	890-910	AGUUCUTUCGCAUGUAAGAAACC	1894	888-910
AD-1948312	UUUCUUACAUGCGAAAGAACU	414	890-910	AGUUCUTUCGCAUGUAAGAAACC	1895	888-910
AD-1948313	UUCUUACAUGCGAAAGAACAU	415	891-911	ATGUTCTUUCGCAUGUAAGAAAC	1896	889-911
AD-1948314	UUCUUACAUGCGAAAGAACAU	416	891-911	AUGUTCTUUCGCAUGUAAGAAAC	1897	889-911
AD-1948315	UCUUACAUGCGAAAGAACAGU	417	892-912	ACUGTUCUUUCGCAUGUAAGAAA	1898	890-912
AD-1948316	UACAUGCGAAAGAACAGGGAU	418	895-915	ATCCCUGUUCUTUCGCAUGUAAG	1899	893-915
AD-1948317	ACAUGCGAAAGAACAGGGAAU	419	896-916	ATUCCCTGUUCTUUCGCAUGUAA	1900	894-916
AD-1948318	ACAUGCGAAAGAACAGGGAAU	420	896-916	AUUCCCTGUUCUUUCGCAUGUAA	1901	894-916
AD-1948319	CAUGCGAAAGAACAGGGAAAU	421	897-917	ATUUCCCUGUUCUUUCGCAUGUA	1902	895-917
AD-1948320	AUGCGAAAGAACAGGGAAAGU	422	898-918	ACUUTCCCUGUTCUUUCGCAUGU	1903	896-918

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948321	UGCGAAAGAACA GGGAAAGAU	423	899-919	ATCUTUCCCUGTU CUUUCGCAUG	1904	897-919
AD-1948322	GCGAAAGAACAG GGAAAGAAU	424	900-920	ATUCTUTCCCUGU UCUUUCGCAU	1905	898-920
AD-1948323	GCGAAAGAACAG GGAAAGAAU	425	900-920	AUUCTUTCCCUGU UCUUUCGCAU	1906	898-920
AD-1948324	GAAAGAACAGGG AAAGAAGUU	426	902-922	AACUTCTUUCCCU GUUCUUUCGC	1907	900-922
AD-1948325	GAAAGAACAGGG AAAGAAGUU	427	902-922	AACUTCTUUCCCU GUUCUUUCGC	1908	900-922
AD-1948326	AAAGAACAGGGA AAGAAGUCU	428	903-923	AGACTUCUUUCCC UGUUCUUUCG	1909	901-923
AD-1948327	AAGAACAGGGAA AGAAGUCUU	429	904-924	AAGACUTCUUUCC CUGUUCUUUC	1910	902-924
AD-1948328	AAGAACAGGGAA AGAAGUCUU	430	904-924	AAGACUTCUUUCC CUGUUCUUUC	1911	902-924
AD-1948329	AGAACAGGGAAA GAAGUCUUU	431	905-925	AAAGACTUCUUTC CCUGUUCUUU	1912	903-925
AD-1948330	AGAACAGGGAAA GAAGUCUUU	432	905-925	AAAGACTUCUUU CCCUGUUCUUU	1913	903-925
AD-1948331	GAACAGGGAAAG AAGUCUUGU	433	906-926	ACAAGACUUCUT UCCCUGUUCUU	1914	904-926
AD-1948332	ACAGGGAAAGAA GUCUUGGAU	434	908-928	ATCCAAGACUUCU UUCCCUGUUC	1915	906-928
AD-1948333	CAGGGAAAGAAG UCUUGGAAU	435	909-929	ATUCCAAGACUTC UUUCCCUGUU	1916	907-929
AD-1948334	CAGGGAAAGAAG UCUUGGAAU	436	909-929	AUUCCAAGACUU CUUUCCCUGUU	1917	907-929
AD-1948335	AGGGAAAGAAG UCUUGGAAAU	437	910-930	ATUUCCAAGACTU CUUUCCCUGU	1918	908-930
AD-1948336	AGGGAAAGAAG UCUUGGAAAU	438	910-930	AUUUCCAAGACU UCUUUCCCUGU	1919	908-930
AD-1948337	GGGAAAGAAGUC UUGGAAAAU	439	911-931	ATUUTCCAAGACU UCUUUCCCUG	1920	909-931
AD-1948338	GGAAAGAAGUCU UGGAAAAAU	440	912-932	ATUUTUCCAAGAC UUCUUUCCCU	1921	910-932
AD-1948339	GAAAGAAGUCUU GGAAAAAAU	441	913-933	ATUUTUTCCAAGA CUUCUUUCCC	1922	911-933
AD-1948340	GAAAGAAGUCUU GGAAAAAAU	442	913-933	AUUUTUTCCAAGA CUUCUUUCCC	1923	911-933
AD-1948341	AAAGAAGUCUUG GAAAAAAAU	443	914-934	ATUUTUTUCCAAG ACUUCUUUCC	1924	912-934
AD-1948342	AAAGAAGUCUUG GAAAAAAAU	444	914-934	AUUUTUTUCCAAG ACUUCUUUCC	1925	912-934
AD-1948343	AAGAAGUCUUGG AAAAAAAUU	445	915-935	AAUUTUTUUCCAA GACUUCUUUC	1926	913-935
AD-1948344	AAGAAGUCUUGG AAAAAAAUU	446	915-935	AAUUTUTUUCCAA GACUUCUUUC	1927	913-935

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948345	AAGUCUUGGAAAAAAAUUUAU	447	918-938	ATAAAUTUUUUTCCAAGACUUCU	1928	916-938
AD-1948346	AGUCUUGGAAAAAAAUUUACU	448	919-939	AGUAAATUUUUTUCCAAGACUUC	1929	917-939
AD-1948347	ACUUUUUUCUAAGAAGAUCUU	449	937-957	AAGATCTUCUUAGAAAAAAGUAA	1930	935-957
AD-1948348	ACUUUUUUCUAAGAAGAUCUU	450	937-957	AAGATCTUCUUAGAAAAAAGUAA	1931	935-957
AD-1948349	CUUUUUUCUAAGAAGAUCUGU	451	938-958	ACAGAUCUUCUTAGAAAAAAGUA	1932	936-958
AD-1948350	UUUUUUCUAAGAAGAUCUGGU	452	939-959	ACCAGATCUUCTUAGAAAAAAGU	1933	937-959
AD-1948351	UUUUUCUAAGAAGAUCUGGUU	453	940-960	AACCAGAUCUUCUUAGAAAAAAG	1934	938-960
AD-1948352	UUUUUCUAAGAAGAUCUGGUU	454	940-960	AACCAGAUCUUCUUAGAAAAAAG	1935	938-960
AD-1948353	UUUUCUAAGAAGAUCUGGUUU	455	941-961	AAACCAGAUCUTCUUAGAAAAAA	1936	939-961
AD-1948354	UUUCUAAGAAGAUCUGGUUUU	456	942-962	AAAACCAGAUCTUCUUAGAAAAA	1937	940-962
AD-1948355	UUUCUAAGAAGAUCUGGUUUU	457	942-962	AAAACCAGAUCUUCUUAGAAAAA	1938	940-962
AD-1948356	UUCUAAGAAGAUCUGGUUUAU	458	943-963	ATAAACCAGAUCUUCUUAGAAAA	1939	941-963
AD-1948357	UCUAAGAAGAUCUGGUUUAUU	459	944-964	AAUAAACCAGATCUUCUUAGAAA	1940	942-964
AD-1948358	CUAAGAAGAUCUGGUUUAUAU	460	945-965	ATAUAAACCAGAUCUUCUUAGAA	1941	943-965
AD-1948359	UAAGAAGAUCUGGUUUAUAUU	461	946-966	AAUATAAACCAGAUCUUCUUAGA	1942	944-966
AD-1948360	AAGAAGAUCUGGUUUAUAUUU	462	947-967	AAAUAUAAACCAGAUCUUCUUAG	1943	945-967
AD-1948361	AAGAUCUGGUUUAUAUUUUUU	463	950-970	AAAAAATAUAAACCAGAUCUUCU	1944	948-970
AD-1948362	AGAUCUGGUUUAUAUUUUUCU	464	951-971	AGAAAAAUAUAAACCAGAUCUUC	1945	949-971
AD-1948363	AUCUGGUUUAUAUUUUUCUAU	465	953-973	ATAGAAAAAUATAAACCAGAUCU	1946	951-973
AD-1948364	UCUGGUUUAUAUUUUUCUACU	466	954-974	AGUAGAAAAAUAUAAACCAGAUC	1947	952-974
AD-1948365	UUUAUAUUUUUCUACUAAAGU	467	959-979	ACUUTAGUAGAAAAUAUAAACC	1948	957-979
AD-1948366	UCAAAGGAACCGCGGCAUUUU	468	984-1004	AAAATGCCGCGGUUCCUUUGAUG	1949	982-1004
AD-1948367	AAGGAACCGCGGCAUUUGCAU	469	987-1007	ATGCAAAUGCCGCGGUUCCUUUG	1950	985-1007
AD-1948368	AGGAACCGCGGCAUUUGCAGU	470	988-1008	ACUGCAAAUGCCGCGGUUCCUUU	1951	986-1008

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948369	GAACCGCGGCAUUUGCAGUUU	471	990-1010	AAACTGCAAAUGCCGCGGUUCCU	1952	988-1010
AD-1948370	AACCGCGGCAUUUGCAGUUUU	472	991-1011	AAAACUGCAAATGCCGCGGUUCC	1953	989-1011
AD-1948371	CCGCGGCAUUUGCAGUUUUUU	473	993-1013	AAAAAACUGCAAAUGCCGCGGUU	1954	991-1013
AD-1948372	GCGGCAUUUGCAGUUUUUCAU	474	995-1015	ATGAAAAACUGCAAAUGCCGCGG	1955	993-1015
AD-1948373	CGGCAUUUGCAGUUUUUCAGU	475	996-1016	ACUGAAAAACUGCAAAUGCCGCG	1956	994-1016
AD-1948374	GGCAUUUGCAGUUUUUCAGCU	476	997-1017	AGCUGAAAAACTGCAAAUGCCGC	1957	995-1017
AD-1948375	GCAUUUGCAGUUUUUCAGCGU	477	998-1018	ACGCTGAAAAACUGCAAAUGCCG	1958	996-1018
AD-1948376	GCAUUUGCAGUUUUUCAGCGU	478	998-1018	ACGCTGAAAAACUGCAAAUGCCG	1959	996-1018
AD-1948377	CAUUUGCAGUUUUUCAGCGAU	479	999-1019	ATCGCUGAAAAACUGCAAAUGCC	1960	997-1019
AD-1948378	AUUUGCAGUUUUUCAGCGAAU	480	1000-1020	ATUCGCTGAAAAACUGCAAAUGC	1961	998-1020
AD-1948379	AUUUGCAGUUUUUCAGCGAAU	481	1000-1020	AUUCGCTGAAAAACUGCAAAUGC	1962	998-1020
AD-1948380	UUUGCAGUUUUUCAGCGAAUU	482	1001-1021	AAUUCGCUGAAAAACUGCAAAUG	1963	999-1021
AD-1948381	UUGCAGUUUUUCAGCGAAUUU	483	1002-1022	AAAUTCGCUGAAAAACUGCAAAU	1964	1000-1022
AD-1948382	UGCAGUUUUUCAGCGAAUUUU	484	1003-1023	AAAATUCGCUGAAAAACUGCAAA	1965	1001-1023
AD-1948383	GCAGUUUUUCAGCGAAUUUGU	485	1004-1024	ACAAAUTCGCUGAAAAACUGCAA	1966	1002-1024
AD-1948384	CAGUUUUUCAGCGAAUUUGGU	486	1005-1025	ACCAAATUCGCTGAAAAACUGCA	1967	1003-1025
AD-1948385	AGUUUUUCAGCGAAUUUGGCU	487	1006-1026	AGCCAAAUUCGCUGAAAAACUGC	1968	1004-1026
AD-1948386	GUUUUUCAGCGAAUUUGGCAU	488	1007-1027	ATGCCAAAUUCGCUGAAAAACUG	1969	1005-1027
AD-1948387	UUUUUCAGCGAAUUUGGCAAU	489	1008-1028	ATUGCCAAAUUCGCUGAAAAACU	1970	1006-1028
AD-1948388	UUUUUCAGCGAAUUUGGCAAU	490	1008-1028	AUUGCCAAAUUCGCUGAAAAACU	1971	1006-1028
AD-1948389	UUUUCAGCGAAUUUGGCAAUU	491	1009-1029	AAUUGCCAAAUTCGCUGAAAAAC	1972	1007-1029
AD-1948390	UUUCAGCGAAUUUGGCAAUAU	492	1010-1030	ATAUTGCCAAATUCGCUGAAAAA	1973	1008-1030
AD-1948391	UUCAGCGAAUUUGGCAAUAGU	493	1011-1031	ACUATUGCCAAAUUCGCUGAAAA	1974	1009-1031
AD-1948392	UCAGCGAAUUUGGCAAUAGUU	494	1012-1032	AACUAUTGCCAAAUUCGCUGAAA	1975	1010-1032

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948393	CAGCGAAUUUGGCAAUAGUGU	495	1013-1033	ACACTATUGCCAAAUUCGCUGAA	1976	1011-1033
AD-1948394	AGCGAAUUUGGCAAUAGUGAU	496	1014-1034	ATCACUAUUGCCAAAUUCGCUGA	1977	1012-1034
AD-1948395	GCGAAUUUGGCAAUAGUGAUU	497	1015-1035	AAUCACTAUUGCCAAAUUCGCUG	1978	1013-1035
AD-1948396	GCGAAUUUGGCAAUAGUGAUU	498	1015-1035	AAUCACTAUUGCCAAAUUCGCUG	1979	1013-1035
AD-1948397	CGAAUUUGGCAAUAGUGAUAU	499	1016-1036	ATAUCACUAUUGCCAAAUUCGCU	1980	1014-1036
AD-1948398	GAAUUUGGCAAUAGUGAUAUU	500	1017-1037	AAUATCACUAUTGCCAAAUUCGC	1981	1015-1037
AD-1948399	GAAUUUGGCAAUAGUGAUAUU	501	1017-1037	AAUATCACUAUUGCCAAAUUCGC	1982	1015-1037
AD-1948400	AAUUUGGCAAUAGUGAUAUUU	502	1018-1038	AAAUAUCACUATUGCCAAAUUCG	1983	1016-1038
AD-1948401	AUUUGGCAAUAGUGAUAUUUU	503	1019-1039	AAAATATCACUAUUGCCAAAUUC	1984	1017-1039
AD-1948402	AUUUGGCAAUAGUGAUAUUUU	504	1019-1039	AAAATATCACUAUUGCCAAAUUC	1985	1017-1039
AD-1948403	UUGGCAAUAGUGAUAUUUAUU	505	1021-1041	AAUAAATAUCACUAUUGCCAAAU	1986	1019-1041
AD-1948404	UGGCAAUAGUGAUAUUUAUGU	506	1022-1042	ACAUAAAUAUCACUAUUGCCAAA	1987	1020-1042
AD-1948405	GGCAAUAGUGAUAUUUAUGUU	507	1023-1043	AACATAAAUAUCACUAUUGCCAA	1988	1021-1043
AD-1948406	GCAAUAGUGAUAUUUAUGUGU	508	1024-1044	ACACAUAAAUATCACUAUUGCCA	1989	1022-1044
AD-1948407	CAAUAGUGAUAUUUAUGUGUU	509	1025-1045	AACACATAAAUAUCACUAUUGCC	1990	1023-1045
AD-1948408	AAUAGUGAUAUUUAUGUGUCU	510	1026-1046	AGACACAUAAATAUCACUAUUGC	1991	1024-1046
AD-1948409	AAUAGUGAUAUUUAUGUGUCU	511	1026-1046	AGACACAUAAAUAUCACUAUUGC	1992	1024-1046
AD-1948410	AACAUGGAGCACCGACUAACU	512	1063-1083	AGUUAGTCGGUGCUCCAUGUUUU	1993	1061-1083
AD-1948411	AACAUGGAGCACCGACUAACU	513	1063-1083	AGUUAGTCGGUGCUCCAUGUUUU	1994	1061-1083
AD-1948412	ACAUGGAGCACCGACUAACUU	514	1064-1084	AAGUTAGUCGGTGCUCCAUGUUU	1995	1062-1084
AD-1948413	CAUGGAGCACCGACUAACUAU	515	1065-1085	ATAGTUAGUCGGUGCUCCAUGUU	1996	1063-1085
AD-1948414	CAUGGAGCACCGACUAACUAU	516	1065-1085	AUAGTUAGUCGGUGCUCCAUGUU	1997	1063-1085
AD-1948415	AUGGAGCACCGACUAACUAUU	517	1066-1086	AAUAGUTAGUCGGUGCUCCAUGU	1998	1064-1086
AD-1948416	AUGGAGCACCGACUAACUAUU	518	1066-1086	AAUAGUTAGUCGGUGCUCCAUGU	1999	1064-1086

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948417	UGGAGCACCGAC UAACUAUGU	519	1067-1087	ACAUAGTUAGUC GGUGCUCCAUG	2000	1065-1087
AD-1948418	GGAGCACCGACU AACUAUGGU	520	1068-1088	ACCATAGUUAGTC GGUGCUCCAU	2001	1066-1088
AD-1948419	GAGCACCGACUA ACUAUGGAU	521	1069-1089	ATCCAUAGUUAG UCGGUGCUCCA	2002	1067-1089
AD-1948420	AGCACCGACUAA CUAUGGAUU	522	1070-1090	AAUCCATAGUUA GUCGGUGCUCC	2003	1068-1090
AD-1948421	GCACCGACUAAC UAUGGAUUU	523	1071-1091	AAAUCCAUAGUT AGUCGGUGCUC	2004	1069-1091
AD-1948422	GCACCGACUAAC UAUGGAUUU	524	1071-1091	AAAUCCAUAGUU AGUCGGUGCUC	2005	1069-1091
AD-1948423	CACCGACUAACU AUGGAUUCU	525	1072-1092	AGAATCCAUAGTU AGUCGGUGCU	2006	1070-1092
AD-1948424	ACCGACUAACUA UGGAUUCUU	526	1073-1093	AAGAAUCCAUAG UUAGUCGGUGC	2007	1071-1093
AD-1948425	CCGACUAACUAU GGAUUCUGU	527	1074-1094	ACAGAATCCAUA GUUAGUCGGUG	2008	1072-1094
AD-1948426	CGACUAACUAUG GAUUCUGCU	528	1075-1095	AGCAGAAUCCAT AGUUAGUCGGU	2009	1073-1095
AD-1948427	CGACUAACUAUG GAUUCUGCU	529	1075-1095	AGCAGAAUCCAU AGUUAGUCGGU	2010	1073-1095
AD-1948428	GACUAACUAUGG AUUCUGCUU	530	1076-1096	AAGCAGAAUCCA UAGUUAGUCGG	2011	1074-1096
AD-1948429	GACUAACUAUGG AUUCUGCUU	531	1076-1096	AAGCAGAAUCCA UAGUUAGUCGG	2012	1074-1096
AD-1948430	ACUAACUAUGGA UUCUGCUUU	532	1077-1097	AAAGCAGAAUCC AUAGUUAGUCG	2013	1075-1097
AD-1948431	CUAACUAUGGAU UCUGCUUUU	533	1078-1098	AAAAGCAGAAUC CAUAGUUAGUC	2014	1076-1098
AD-1948432	CUAACUAUGGAU UCUGCUUUU	534	1078-1098	AAAAGCAGAAUC CAUAGUUAGUC	2015	1076-1098
AD-1948433	UAACUAUGGAUU CUGCUUUAU	535	1079-1099	ATAAAGCAGAATC CAUAGUUAGU	2016	1077-1099
AD-1948434	AACUAUGGAUUC UGCUUUAAU	536	1080-1100	ATUAAAGCAGAA UCCAUAGUUAG	2017	1078-1100
AD-1948435	ACUAUGGAUUCU GCUUUAAGU	537	1081-1101	ACUUAAAGCAGA AUCCAUAGUUA	2018	1079-1101
AD-1948436	CUAUGGAUUCUG CUUUAAGCU	538	1082-1102	AGCUTAAAGCAG AAUCCAUAGUU	2019	1080-1102
AD-1948437	UAUGGAUUCUGC UUUAAGCCU	539	1083-1103	AGGCTUAAAGCA GAAUCCAUAGU	2020	1081-1103
AD-1948438	AUGGAUUCUGCU UUAAGCCUU	540	1084-1104	AAGGCUTAAAGC AGAAUCCAUAG	2021	1082-1104
AD-1948439	AUGGAUUCUGCU UUAAGCCUU	541	1084-1104	AAGGCUTAAAGC AGAAUCCAUAG	2022	1082-1104
AD-1948440	UGGAUUCUGCUU UAAGCCUAU	542	1085-1105	ATAGGCTUAAAGC AGAAUCCAUA	2023	1083-1105

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948441	UGGAUUCUGCUUUAAGCCUAU	543	1085-1105	AUAGGCTUAAAGCAGAAUCCAUA	2024	1083-1105
AD-1948442	GGAUUCUGCUUUAAGCCUAAU	544	1086-1106	ATUAGGCUUAAAGCAGAAUCCAU	2025	1084-1106
AD-1948443	GAUUCUGCUUUAAGCCUAACU	545	1087-1107	AGUUAGGCUUAAAGCAGAAUCCA	2026	1085-1107
AD-1948444	AUUCUGCUUUAAGCCUAACAU	546	1088-1108	ATGUTAGGCUUAAAGCAGAAUCC	2027	1086-1108
AD-1948445	UUCUGCUUUAAGCCUAACAAU	547	1089-1109	ATUGTUAGGCUTAAAGCAGAAUC	2028	1087-1109
AD-1948446	UUCUGCUUUAAGCCUAACAAU	548	1089-1109	AUUGTUAGGCUUAAAGCAGAAUC	2029	1087-1109
AD-1948447	UCUGCUUUAAGCCUAACAAAU	549	1090-1110	ATUUGUTAGGCTUAAAGCAGAAU	2030	1088-1110
AD-1948448	UCUGCUUUAAGCCUAACAAAU	550	1090-1110	AUUUGUTAGGCUUAAAGCAGAAU	2031	1088-1110
AD-1948449	CUGCUUUAAGCCUAACAAAGU	551	1091-1111	ACUUTGTUAGGCUUAAAGCAGAA	2032	1089-1111
AD-1948450	CUGCUUUAAGCCUAACAAAGU	552	1091-1111	ACUUTGTUAGGCUUAAAGCAGAA	2033	1089-1111
AD-1948451	UGCUUUAAGCCUAACAAAGCU	553	1092-1112	AGCUTUGUUAGGCUUAAAGCAGA	2034	1090-1112
AD-1948452	CGAGACCUGAAAAUGCUCUGU	554	1122-1142	ACAGAGCAUUUTCAGGUCUCGGG	2035	1120-1142
AD-1948453	GAGACCUGAAAAUGCUCUGUU	555	1123-1143	AACAGAGCAUUTUCAGGUCUCGG	2036	1121-1143
AD-1948454	AGACCUGAAAAUGCUCUGUGU	556	1124-1144	ACACAGAGCAUTUUCAGGUCUCG	2037	1122-1144
AD-1948455	AGACCUGAAAAUGCUCUGUGU	557	1124-1144	ACACAGAGCAUUUUCAGGUCUCG	2038	1122-1144
AD-1948456	GACCUGAAAAUGCUCUGUGCU	558	1125-1145	AGCACAGAGCATUUUCAGGUCUC	2039	1123-1145
AD-1948457	ACCUGAAAAUGCUCUGUGCAU	559	1126-1146	ATGCACAGAGCAUUUUCAGGUCU	2040	1124-1146
AD-1948458	ACCUGAAAAUGCUCUGUGCAU	560	1126-1146	AUGCACAGAGCAUUUUCAGGUCU	2041	1124-1146
AD-1948459	CCUGAAAAUGCUCUGUGCAGU	561	1127-1147	ACUGCACAGAGCAUUUUCAGGUC	2042	1125-1147
AD-1948460	CUGAAAAUGCUCUGUGCAGAU	562	1128-1148	ATCUGCACAGAGCAUUUUCAGGU	2043	1126-1148
AD-1948461	CUGAAAAUGCUCUGUGCAGAU	563	1128-1148	AUCUGCACAGAGCAUUUUCAGGU	2044	1126-1148
AD-1948462	UGAAAAUGCUCUGUGCAGAAU	564	1129-1149	ATUCTGCACAGAGCAUUUUCAGG	2045	1127-1149
AD-1948463	GAAAAUGCUCUGUGCAGAAGU	565	1130-1150	ACUUCUGCACAGAGCAUUUUCAG	2046	1128-1150
AD-1948464	AAAAUGCUCUGUGCAGAAGAU	566	1131-1151	ATCUTCTGCACAGAGCAUUUUCA	2047	1129-1151

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948465	AAAAUGCUCUGUGCAGAAGAU	567	1131-1151	AUCUTCTGCACAGAGCAUUUUCA	2048	1129-1151
AD-1948466	AAAUGCUCUGUGCAGAAGAAU	568	1132-1152	ATUCTUCUGCACAGAGCAUUUUC	2049	1130-1152
AD-1948467	AAUGCUCUGUGCAGAAGAAGU	569	1133-1153	ACUUCUTCUGCACAGAGCAUUUU	2050	1131-1153
AD-1948468	AUGCUCUGUGCAGAAGAAGAU	570	1134-1154	ATCUTCTUCUGCACAGAGCAUUU	2051	1132-1154
AD-1948469	AUGCUCUGUGCAGAAGAAGAU	571	1134-1154	AUCUTCTUCUGCACAGAGCAUUU	2052	1132-1154
AD-1948470	CUCUGUGCAGAAGAAGAGCAU	572	1137-1157	ATGCTCTUCUUCUGCACAGAGCA	2053	1135-1157
AD-1948471	CUCUGUGCAGAAGAAGAGCAU	573	1137-1157	AUGCTCTUCUUCUGCACAGAGCA	2054	1135-1157
AD-1948472	UCUGUGCAGAAGAAGAGCAGU	574	1138-1158	ACUGCUCUUCUTCUGCACAGAGC	2055	1136-1158
AD-1948473	UGUGCAGAAGAAGAGCAGAGU	575	1140-1160	ACUCTGCUCUUCUUCUGCACAGA	2056	1138-1160
AD-1948474	GUGCAGAAGAAGAGCAGAGUU	576	1141-1161	AACUCUGCUCUTCUUCUGCACAG	2057	1139-1161
AD-1948475	UGCAGAAGAAGAGCAGAGUAU	577	1142-1162	ATACTCTGCUCTUCUUCUGCACA	2058	1140-1162
AD-1948476	UGCAGAAGAAGAGCAGAGUAU	578	1142-1162	AUACTCTGCUCUUCUUCUGCACA	2059	1140-1162
AD-1948477	GCAGAAGAAGAGCAGAGUAGU	579	1143-1163	ACUACUCUGCUCUUCUUCUGCAC	2060	1141-1163
AD-1948478	CAGAAGAAGAGCAGAGUAGGU	580	1144-1164	ACCUACTCUGCTCUUCUUCUGCA	2061	1142-1164
AD-1948479	AGAAGAAGAGCAGAGUAGGAU	581	1145-1165	ATCCTACUCUGCUCUUCUUCUGC	2062	1143-1165
AD-1948480	GAAGAAGAGCAGAGUAGGACU	582	1146-1166	AGUCCUACUCUGCUCUUCUUCUG	2063	1144-1166
AD-1948481	GAAGAAGAGCAGAGUAGGACU	583	1146-1166	AGUCCUACUCUGCUCUUCUUCUG	2064	1144-1166
AD-1948482	AGAGCAGAGUAGGACGUGCUU	584	1151-1171	AAGCACGUCCUACUCUGCUCUUC	2065	1149-1171
AD-1948483	AGAGUAGGACGUGCUGGGUGU	585	1156-1176	ACACCCAGCACGUCCUACUCUGC	2066	1154-1176
AD-1948484	GAGUAGGACGUGCUGGGUGAU	586	1157-1177	ATCACCCAGCACGUCCUACUCUG	2067	1155-1177
AD-1948485	CGUGCUGGGUGACCGCGAUUU	587	1165-1185	AAAUCGCGGUCACCCAGCACGUC	2068	1163-1185
AD-1948486	GUGCUGGGUGACCGCGAUUAU	588	1166-1186	ATAATCGCGGUCACCCAGCACGU	2069	1164-1186
AD-1948487	UGCUGGGUGACCGCGAUUAGU	589	1167-1187	ACUAAUCGCGGTCACCCAGCACG	2070	1165-1187
AD-1948488	CUGGGUGACCGCGAUUAGAUU	590	1169-1189	AAUCTAAUCGCGGUCACCCAGCA	2071	1167-1189

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948489	UGGGUGACCGCG AUUAGAUUU	591	1170-1190	AAAUCUAAUCGC GGUCACCCAGC	2072	1168-1190
AD-1948490	GGGUGACCGCGA UUAGAUUGU	592	1171-1191	ACAATCTAAUCGC GGUCACCCAG	2073	1169-1191
AD-1948491	GGGUGACCGCGA UUAGAUUGU	593	1171-1191	ACAATCTAAUCGC GGUCACCCAG	2074	1169-1191
AD-1948492	GGUGACCGCGAU UAGAUUGCU	594	1172-1192	AGCAAUCUAAUC GCGGUCACCCA	2075	1170-1192
AD-1948493	GUGACCGCGAUU AGAUUGCUU	595	1173-1193	AAGCAATCUAATC GCGGUCACCC	2076	1171-1193
AD-1948494	UGACCGCGAUUA GAUUGCUUU	596	1174-1194	AAAGCAAUCUAA UCGCGGUCACC	2077	1172-1194
AD-1948495	GACCGCGAUUAG AUUGCUUAU	597	1175-1195	ATAAGCAAUCUA AUCGCGGUCAC	2078	1173-1195
AD-1948496	GACCGCGAUUAG AUUGCUUAU	598	1175-1195	AUAAGCAAUCUA AUCGCGGUCAC	2079	1173-1195
AD-1948497	ACCGCGAUUAGA UUGCUUAAU	599	1176-1196	ATUAAGCAAUCTA AUCGCGGUCA	2080	1174-1196
AD-1948498	CCGCGAUUAGAU UGCUUAAGU	600	1177-1197	ACUUAAGCAAUC UAAUCGCGGUC	2081	1175-1197
AD-1948499	CGCGAUUAGAUU GCUUAAGUU	601	1178-1198	AACUTAAGCAATC UAAUCGCGGU	2082	1176-1198
AD-1948500	GCGAUUAGAUUG CUUAAGUAU	602	1179-1199	ATACTUAAGCAAU CUAAUCGCGG	2083	1177-1199
AD-1948501	CGAUUAGAUUGC UUAAGUAUU	603	1180-1200	AAUACUTAAGCA AUCUAAUCGCG	2084	1178-1200
AD-1948502	GAUUAGAUUGCU UAAGUAUGU	604	1181-1201	ACAUACTUAAGC AAUCUAAUCGC	2085	1179-1201
AD-1948503	AUUAGAUUGCUU AAGUAUGGU	605	1182-1202	ACCATACUUAAGC AAUCUAAUCG	2086	1180-1202
AD-1948504	UUAGAUUGCUUA AGUAUGGCU	606	1183-1203	AGCCAUACUUAA GCAAUCUAAUC	2087	1181-1203
AD-1948505	UAGAUUGCUUAA GUAUGGCAU	607	1184-1204	ATGCCATACUUAA GCAAUCUAAU	2088	1182-1204
AD-1948506	UAGAUUGCUUAA GUAUGGCAU	608	1184-1204	AUGCCATACUUA AGCAAUCUAAU	2089	1182-1204
AD-1948507	AGAUUGCUUAAG UAUGGCAUU	609	1185-1205	AAUGCCAUACUT AAGCAAUCUAA	2090	1183-1205
AD-1948508	AGAUUGCUUAAG UAUGGCAUU	610	1185-1205	AAUGCCAUACUU AAGCAAUCUAA	2091	1183-1205
AD-1948509	GAUUGCUUAAGU AUGGCAUGU	611	1186-1206	ACAUGCCAUACTU AAGCAAUCUA	2092	1184-1206
AD-1948510	AUUGCUUAAGUA UGGCAUGCU	612	1187-1207	AGCATGCCAUACU UAAGCAAUCU	2093	1185-1207
AD-1948511	UUGCUUAAGUAU GGCAUGCAU	613	1188-1208	ATGCAUGCCAUAC UUAAGCAAUC	2094	1186-1208
AD-1948512	UGCUUAAGUAUG GCAUGCAGU	614	1189-1209	ACUGCATGCCATA CUUAAGCAAU	2095	1187-1209

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948513	UGCUUAAGUAUGGCAUGCAGU	615	1189-1209	ACUGCATGCCAUACUUAAGCAAU	2096	1187-1209
AD-1948514	GCUUAAGUAUGGCAUGCAGCU	616	1190-1210	AGCUGCAUGCCAUACUUAAGCAA	2097	1188-1210
AD-1948515	GCUUAAGUAUGGCAUGCAGCU	617	1190-1210	AGCUGCAUGCCAUACUUAAGCAA	2098	1188-1210
AD-1948516	CUUAAGUAUGGCAUGCAGCUU	618	1191-1211	AAGCUGCAUGCCAUACUUAAGCA	2099	1189-1211
AD-1948517	UAAGUAUGGCAUGCAGCUGUU	619	1193-1213	AACAGCUGCAUGCCAUACUUAAG	2100	1191-1213
AD-1948518	UAAGUAUGGCAUGCAGCUGUU	620	1193-1213	AACAGCUGCAUGCCAUACUUAAG	2101	1191-1213
AD-1948519	AAGUAUGGCAUGCAGCUGUAU	621	1194-1214	ATACAGCUGCATGCCAUACUUAA	2102	1192-1214
AD-1948520	AUGGCAUGCAGCUGUACCAGU	622	1198-1218	ACUGGUACAGCTGCAUGCCAUAC	2103	1196-1218
AD-1948521	UGGCAUGCAGCUGUACCAGAU	623	1199-1219	ATCUGGTACAGCUGCAUGCCAUA	2104	1197-1219
AD-1948522	UGGCAUGCAGCUGUACCAGAU	624	1199-1219	AUCUGGTACAGCUGCAUGCCAUA	2105	1197-1219
AD-1948523	GGCAUGCAGCUGUACCAGAAU	625	1200-1220	ATUCTGGUACAGCUGCAUGCCAU	2106	1198-1220
AD-1948524	GCAUGCAGCUGUACCAGAAUU	626	1201-1221	AAUUCUGGUACAGCUGCAUGCCA	2107	1199-1221
AD-1948525	AUGCAGCUGUACCAGAAUUAU	627	1203-1223	ATAATUCUGGUACAGCUGCAUGC	2108	1201-1223
AD-1948526	UGCAGCUGUACCAGAAUUAUU	628	1204-1224	AAUAAUTCUGGTACAGCUGCAUG	2109	1202-1224
AD-1948527	GCAGCUGUACCAGAAUUAUAU	629	1205-1225	ATAUAATUCUGGUACAGCUGCAU	2110	1203-1225
AD-1948528	CAGCUGUACCAGAAUUAUAUU	630	1206-1226	AAUATAAUUCUGGUACAGCUGCA	2111	1204-1226
AD-1948529	AGCUGUACCAGAAUUAUAUGU	631	1207-1227	ACAUAUAAUUCTGGUACAGCUGC	2112	1205-1227
AD-1948530	GCUGUACCAGAAUUAUAUGCU	632	1208-1228	AGCATATAAUUCUGGUACAGCUG	2113	1206-1228
AD-1948531	CUGUACCAGAAUUAUAUGCAU	633	1209-1229	ATGCAUAUAAUTCUGGUACAGCU	2114	1207-1229
AD-1948532	CUGUACCAGAAUUAUAUGCAU	634	1209-1229	AUGCAUAUAAUUCUGGUACAGCU	2115	1207-1229
AD-1948533	UGUACCAGAAUUAUAUGCAUU	635	1210-1230	AAUGCATAUAATUCUGGUACAGC	2116	1208-1230
AD-1948534	UGUACCAGAAUUAUAUGCAUU	636	1210-1230	AAUGCATAUAAUUCUGGUACAGC	2117	1208-1230
AD-1948535	GUACCAGAAUUAUAUGCAUCU	637	1211-1231	AGAUGCAUAUAAUUCUGGUACAG	2118	1209-1231
AD-1948536	GUACCAGAAUUAUAUGCAUCU	638	1211-1231	AGAUGCAUAUAAUUCUGGUACAG	2119	1209-1231

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948537	UACCAGAAUUAUAUGCAUCCU	639	1212-1232	AGGATGCAUAUAAUUCUGGUACA	2120	1210-1232
AD-1948538	ACCAGAAUUAUAUGCAUCCAU	640	1213-1233	ATGGAUGCAUATAAUUCUGGUAC	2121	1211-1233
AD-1948539	CCAGAAUUAUAUGCAUCCAUU	641	1214-1234	AAUGGAUGCAUAUAAUUCUGGUA	2122	1212-1234
AD-1948540	CCAGAAUUAUAUGCAUCCAUU	642	1214-1234	AAUGGAUGCAUAUAAUUCUGGUA	2123	1212-1234
AD-1948541	CAGAAUUAUAUGCAUCCAUAU	643	1215-1235	ATAUGGAUGCATAUAAUUCUGGU	2124	1213-1235
AD-1948542	CAGAAUUAUAUGCAUCCAUAU	644	1215-1235	AUAUGGAUGCAUAUAAUUCUGGU	2125	1213-1235
AD-1948543	AGAAUUAUAUGCAUCCAUAUU	645	1216-1236	AAUATGGAUGCAUAUAAUUCUGG	2126	1214-1236
AD-1948544	GAAUUAUAUGCAUCCAUAUCU	646	1217-1237	AGAUAUGGAUGCAUAUAAUUCUG	2127	1215-1237
AD-1948545	AAUUAUAUGCAUCCAUAUCAU	647	1218-1238	ATGATATGGAUGCAUAUAAUUCU	2128	1216-1238
AD-1948546	AAUUAUAUGCAUCCAUAUCAU	648	1218-1238	AUGATATGGAUGCAUAUAAUUCU	2129	1216-1238
AD-1948547	AUUAUAUGCAUCCAUAUCAAU	649	1219-1239	ATUGAUAUGGATGCAUAUAAUUC	2130	1217-1239
AD-1948548	UUAUAUGCAUCCAUAUCAAGU	650	1220-1240	ACUUGATAUGGAUGCAUAUAAUU	2131	1218-1240
AD-1948549	UAUAUGCAUCCAUAUCAAGGU	651	1221-1241	ACCUTGAUAUGGAUGCAUAUAAU	2132	1219-1241
AD-1948550	UAUAUGCAUCCAUAUCAAGGU	652	1221-1241	ACCUTGAUAUGGAUGCAUAUAAU	2133	1219-1241
AD-1948551	AUAUGCAUCCAUAUCAAGGUU	653	1222-1242	AACCTUGAUAUGGAUGCAUAUAA	2134	1220-1242
AD-1948552	UAUGCAUCCAUAUCAAGGUAU	654	1223-1243	ATACCUTGAUATGGAUGCAUAUA	2135	1221-1243
AD-1948553	UAUGCAUCCAUAUCAAGGUAU	655	1223-1243	AUACCUTGAUAUGGAUGCAUAUA	2136	1221-1243
AD-1948554	AUGCAUCCAUAUCAAGGUAGU	656	1224-1244	ACUACCTUGAUAUGGAUGCAUAU	2137	1222-1244
AD-1948555	UGCAUCCAUAUCAAGGUAGAU	657	1225-1245	ATCUACCUUGATAUGGAUGCAUA	2138	1223-1245
AD-1948556	GCAUCCAUAUCAAGGUAGAAU	658	1226-1246	ATUCTACCUUGAUAUGGAUGCAU	2139	1224-1246
AD-1948557	CAUCCAUAUCAAGGUAGAAGU	659	1227-1247	ACUUCUACCUUGAUAUGGAUGCA	2140	1225-1247
AD-1948558	AUCCAUAUCAAGGUAGAAGUU	660	1228-1248	AACUTCTACCUTGAUAUGGAUGC	2141	1226-1248
AD-1948559	AUCCAUAUCAAGGUAGAAGUU	661	1228-1248	AACUTCTACCUUGAUAUGGAUGC	2142	1226-1248
AD-1948560	UCCAUAUCAAGGUAGAAGUGU	662	1229-1249	ACACTUCUACCTUGAUAUGGAUG	2143	1227-1249

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948561	CCAUAUCAAGGU AGAAGUGGU	663	1230-1250	ACCACUTCUACCU UGAUAUGGAU	2144	1228-1250
AD-1948562	GCUGCAGUUCAC AGAGCAUAU	664	1249-1269	ATAUGCTCUGUGA ACUGCAGCCA	2145	1247-1269
AD-1948563	GCUGCAGUUCAC AGAGCAUAU	665	1249-1269	AUAUGCTCUGUG AACUGCAGCCA	2146	1247-1269
AD-1948564	UGCAGUUCACAG AGCAUAUCU	666	1251-1271	AGAUAUGCUCUG UGAACUGCAGC	2147	1249-1271
AD-1948565	GCAGUUCACAGA GCAUAUCAU	667	1252-1272	ATGATATGCUCTG UGAACUGCAG	2148	1250-1272
AD-1948566	GCAGUUCACAGA GCAUAUCAU	668	1252-1272	AUGATATGCUCUG UGAACUGCAG	2149	1250-1272
AD-1948567	ACCUAUGAGAAG UAUAUCAGU	669	1271-1291	ACUGAUAUACUT CUCAUAGGUGA	2150	1269-1291
AD-1948568	CCUAUGAGAAGU AUAUCAGAU	670	1272-1292	ATCUGATAUACTU CUCAUAGGUG	2151	1270-1292
AD-1948569	CCUAUGAGAAGU AUAUCAGAU	671	1272-1292	AUCUGATAUACU UCUCAUAGGUG	2152	1270-1292
AD-1948570	CUAUGAGAAGUA UAUCAGAGU	672	1273-1293	ACUCTGAUAUAC UUCUCAUAGGU	2153	1271-1293
AD-1948571	CUAUGAGAAGUA UAUCAGAGU	673	1273-1293	ACUCTGAUAUAC UUCUCAUAGGU	2154	1271-1293
AD-1948572	UAUGAGAAGUA UAUCAGAGAU	674	1274-1294	ATCUCUGAUAUA CUUCUCAUAGG	2155	1272-1294
AD-1948573	AUGAGAAGUAU AUCAGAGAAU	675	1275-1295	ATUCTCTGAUATA CUUCUCAUAG	2156	1273-1295
AD-1948574	AUGAGAAGUAU AUCAGAGAAU	676	1275-1295	AUUCTCTGAUAUA CUUCUCAUAG	2157	1273-1295
AD-1948575	CCUGGUAGCAAU GGACUUCUU	677	1298-1318	AAGAAGTCCAUTG CUACCAGGGA	2158	1296-1318
AD-1948576	CCUGGUAGCAAU GGACUUCUU	678	1298-1318	AAGAAGTCCAUU GCUACCAGGGA	2159	1296-1318
AD-1948577	CAAUGGACUUCU CAGGCCAGU	679	1306-1326	ACUGGCCUGAGA AGUCCAUUGCU	2160	1304-1326
AD-1948578	UGGACUUCUCAG GCCAGAAAU	680	1309-1329	ATUUCUGGCCUG AGAAGUCCAUU	2161	1307-1329
AD-1948579	GGACUUCUCAGG CCAGAAAAU	681	1310-1330	ATUUTCTGGCCTG AGAAGUCCAU	2162	1308-1330
AD-1948580	GGACUUCUCAGG CCAGAAAAU	682	1310-1330	AUUUTCTGGCCUG AGAAGUCCAU	2163	1308-1330
AD-1948581	GACUUCUCAGGC CAGAAAAGU	683	1311-1331	ACUUTUCUGGCCU GAGAAGUCCA	2164	1309-1331
AD-1948582	CUUCUCAGGCCA GAAAAGCAU	684	1313-1333	ATGCTUTUCUGGC CUGAGAAGUC	2165	1311-1333
AD-1948583	CUUCUCAGGCCA GAAAAGCAU	685	1313-1333	AUGCTUTUCUGGC CUGAGAAGUC	2166	1311-1333
AD-1948584	CAGGCCAGAAAA GCAGAGUUU	686	1318-1338	AAACTCTGCUUTU CUGGCCUGAG	2167	1316-1338

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948585	CAGGCCAGAAAA GCAGAGUUU	687	1318-1338	AAACTCTGCUUUU CUGGCCUGAG	2168	1316-1338
AD-1948586	AGGCCAGAAAAG CAGAGUUAU	688	1319-1339	ATAACUCUGCUTU UCUGGCCUGA	2169	1317-1339
AD-1948587	GGCCAGAAAAGC AGAGUUAUU	689	1320-1340	AAUAACTCUGCTU UUCUGGCCUG	2170	1318-1340
AD-1948588	GGCCAGAAAAGC AGAGUUAUU	690	1320-1340	AAUAACTCUGCU UUUCUGGCCUG	2171	1318-1340
AD-1948589	GCCAGAAAAGCA GAGUUAUAU	691	1321-1341	ATAUAACUCUGC UUUUCUGGCCU	2172	1319-1341
AD-1948590	CCAGAAAAGCAG AGUUAUAGU	692	1322-1342	ACUATAACUCUGC UUUUCUGGCC	2173	1320-1342
AD-1948591	CAGAAAAGCAGA GUUAUAGAU	693	1323-1343	ATCUAUAACUCTG CUUUUCUGGC	2174	1321-1343
AD-1948592	AGAAAAGCAGAG UUAUAGAAU	694	1324-1344	ATUCTATAACUCU GCUUUUCUGG	2175	1322-1344
AD-1948593	AGAAAAGCAGAG UUAUAGAAU	695	1324-1344	AUUCTATAACUCU GCUUUUCUGG	2176	1322-1344
AD-1948594	GAAAAGCAGAGU UAUAGAAAU	696	1325-1345	ATUUCUAUAACTC UGCUUUUCUG	2177	1323-1345
AD-1948595	GAAAAGCAGAGU UAUAGAAAU	697	1325-1345	AUUUCUAUAACU CUGCUUUUCUG	2178	1323-1345
AD-1948596	AAAAGCAGAGUU AUAGAAAAU	698	1326-1346	ATUUTCTAUAACU CUGCUUUUCU	2179	1324-1346
AD-1948597	AAAAGCAGAGUU AUAGAAAAU	699	1326-1346	AUUUTCTAUAACU CUGCUUUUCU	2180	1324-1346
AD-1948598	AAAGCAGAGUUA UAGAAAAUU	700	1327-1347	AAUUTUCUAUAA CUCUGCUUUUC	2181	1325-1347
AD-1948599	AAGCAGAGUUAU AGAAAAUCU	701	1328-1348	AGAUTUTCUAUA ACUCUGCUUUU	2182	1326-1348
AD-1948600	AAGCAGAGUUAU AGAAAAUCU	702	1328-1348	AGAUTUTCUAUA ACUCUGCUUUU	2183	1326-1348
AD-1948601	AGCAGAGUUAUA GAAAAUCCU	703	1329-1349	AGGATUTUCUATA ACUCUGCUUU	2184	1327-1349
AD-1948602	AGCAGAGUUAUA GAAAAUCCU	704	1329-1349	AGGATUTUCUAU AACUCUGCUUU	2185	1327-1349
AD-1948603	GCAGAGUUAUAG AAAAUCCCU	705	1330-1350	AGGGAUTUUCUA UAACUCUGCUU	2186	1328-1350
AD-1948604	GCAGAGUUAUAG AAAAUCCCU	706	1330-1350	AGGGAUTUUCUA UAACUCUGCUU	2187	1328-1350
AD-1948605	CAGAGUUAUAGA AAAUCCCAU	707	1331-1351	ATGGGATUUUCTA UAACUCUGCU	2188	1329-1351
AD-1948606	CAGAGUUAUAGA AAAUCCCAU	708	1331-1351	AUGGGATUUUCU AUAACUCUGCU	2189	1329-1351
AD-1948607	AGAGUUAUAGA AAAUCCCACU	709	1332-1352	AGUGGGAUUUUC UAUAACUCUGC	2190	1330-1352
AD-1948608	AGAGUUAUAGA AAAUCCCACU	710	1332-1352	AGUGGGAUUUUC UAUAACUCUGC	2191	1330-1352

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948609	GAGUUAUAGAA AAUCCCACUU	711	1333-1353	AAGUGGGAUUUT CUAUAACUCUG	2192	1331-1353
AD-1948610	AGUUAUAGAAA AUCCCACUGU	712	1334-1354	ACAGTGGGAUUT UCUAUAACUCU	2193	1332-1354
AD-1948611	GUUAUAGAAAA UCCCACUGAU	713	1335-1355	ATCAGUGGGAUT UUCUAUAACUC	2194	1333-1355
AD-1948612	UUAUAGAAAAUC CCACUGAAU	714	1336-1356	ATUCAGTGGGATU UUCUAUAACU	2195	1334-1356
AD-1948613	UUAUAGAAAAUC CCACUGAAU	715	1336-1356	AUUCAGTGGGAU UUUCUAUAACU	2196	1334-1356
AD-1948614	UAUAGAAAAUCC CACUGAAGU	716	1337-1357	ACUUCAGUGGGA UUUUCUAUAAC	2197	1335-1357
AD-1948615	AUAGAAAAUCCC ACUGAAGCU	717	1338-1358	AGCUTCAGUGGG AUUUUCUAUAA	2198	1336-1358
AD-1948616	AUAGAAAAUCCC ACUGAAGCU	718	1338-1358	AGCUTCAGUGGG AUUUUCUAUAA	2199	1336-1358
AD-1948617	UAGAAAAUCCCA CUGAAGCCU	719	1339-1359	AGGCTUCAGUGG GAUUUUCUAUA	2200	1337-1359
AD-1948618	GAAAAUCCCACU GAAGCCCUU	720	1341-1361	AAGGGCTUCAGTG GGAUUUUCUA	2201	1339-1361
AD-1948619	GAAAAUCCCACU GAAGCCCUU	721	1341-1361	AAGGGCTUCAGU GGGAUUUUCUA	2202	1339-1361
AD-1948620	AAAAUCCCACUG AAGCCCUUU	722	1342-1362	AAAGGGCUUCAG UGGGAUUUUCU	2203	1340-1362
AD-1948621	AAAUCCCACUGA AGCCCUUUU	723	1343-1363	AAAAGGGCUUCA GUGGGAUUUUC	2204	1341-1363
AD-1948622	UCCCACUGAAGC CCUUUCAGU	724	1346-1366	ACUGAAAGGGCT UCAGUGGGAUU	2205	1344-1366
AD-1948623	CCCACUGAAGCC CUUUCAGUU	725	1347-1367	AACUGAAAGGGC UUCAGUGGGAU	2206	1345-1367
AD-1948624	CACUGAAGCCCU UUCAGUUGU	726	1349-1369	ACAACUGAAAGG GCUUCAGUGGG	2207	1347-1369
AD-1948625	ACUGAAGCCCUU UCAGUUGCU	727	1350-1370	AGCAACTGAAAG GGCUUCAGUGG	2208	1348-1370
AD-1948626	ACUGAAGCCCUU UCAGUUGCU	728	1350-1370	AGCAACTGAAAG GGCUUCAGUGG	2209	1348-1370
AD-1948627	AAGGACUCGCUU GGAGGAAAU	729	1378-1398	ATUUCCTCCAAGC GAGUCCUUCU	2210	1376-1398
AD-1948628	AAGGACUCGCUU GGAGGAAAU	730	1378-1398	AUUUCCTCCAAGC GAGUCCUUCU	2211	1376-1398
AD-1948629	AGGACUCGCUUG GAGGAAAAU	731	1379-1399	ATUUTCCUCCAAG CGAGUCCUUC	2212	1377-1399
AD-1948630	GGACUCGCUUGG AGGAAAAAU	732	1380-1400	ATUUTUCCUCCAA GCGAGUCCUU	2213	1378-1400
AD-1948631	GACUCGCUUGGA GGAAAAAAU	733	1381-1401	ATUUTUTCCUCCA AGCGAGUCCU	2214	1379-1401
AD-1948632	GACUCGCUUGGA GGAAAAAAU	734	1381-1401	AUUUTUTCCUCCA AGCGAGUCCU	2215	1379-1401

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948633	ACUCGCUUGGAG GAAAAAAGU	735	1382-1402	ACUUTUTUCCUCC AAGCGAGUCC	2216	1380-1402
AD-1948634	CUCGCUUGGAGG AAAAAAGGU	736	1383-1403	ACCUTUTUUCCTC CAAGCGAGUC	2217	1381-1403
AD-1948635	UCGCUUGGAGGA AAAAAGGAU	737	1384-1404	ATCCTUTUUUCCU CCAAGCGAGU	2218	1382-1404
AD-1948636	UCGCUUGGAGGA AAAAAGGAU	738	1384-1404	AUCCTUTUUUCCU CCAAGCGAGU	2219	1382-1404
AD-1948637	CGCUUGGAGGAA AAAAGGAUU	739	1385-1405	AAUCCUTUUUUCC UCCAAGCGAG	2220	1383-1405
AD-1948638	GCUUGGAGGAAA AAAGGAUGU	740	1386-1406	ACAUCCTUUUUTC CUCCAAGCGA	2221	1384-1406
AD-1948639	CUUGGAGGAAAA AAGGAUGUU	741	1387-1407	AACATCCUUUUTU CCUCCAAGCG	2222	1385-1407
AD-1948640	UUGGAGGAAAA AAGGAUGUUU	742	1388-1408	AAACAUCCUUUT UUCCUCCAAGC	2223	1386-1408
AD-1948641	UGGAGGAAAAA AGGAUGUUUU	743	1389-1409	AAAACATCCUUTU UUCCUCCAAG	2224	1387-1409
AD-1948642	UGGAGGAAAAA AGGAUGUUUU	744	1389-1409	AAAACATCCUUU UUUCCUCCAAG	2225	1387-1409
AD-1948643	GGAGGAAAAAA GGAUGUUUAU	745	1390-1410	ATAAACAUCCUTU UUUCCUCCAA	2226	1388-1410
AD-1948644	GGAGGAAAAAA GGAUGUUUAU	746	1390-1410	AUAAACAUCCUU UUUUCCUCCAA	2227	1388-1410
AD-1948645	GAGGAAAAAAG GAUGUUUACU	747	1391-1411	AGUAAACAUCCT UUUUUCCUCCA	2228	1389-1411
AD-1948646	AGGAAAAAAGG AUGUUUACGU	748	1392-1412	ACGUAAACAUCC UUUUUUCCUCC	2229	1390-1412
AD-1948647	GGAAAAAAGGA UGUUUACGCU	749	1393-1413	AGCGTAAACAUCC UUUUUUCCUC	2230	1391-1413
AD-1948648	GAAAAAAGGAU GUUUACGCCU	750	1394-1414	AGGCGUAAACAT CCUUUUUUCCU	2231	1392-1414
AD-1948649	AAAAAAGGAUG UUUACGCCUU	751	1395-1415	AAGGCGTAAACA UCCUUUUUUCC	2232	1393-1415
AD-1948650	AAAAAGGAUGU UUACGCCUGU	752	1396-1416	ACAGGCGUAAAC AUCCUUUUUUC	2233	1394-1416
AD-1948651	AAAAGGAUGUU UACGCCUGGU	753	1397-1417	ACCAGGCGUAAA CAUCCUUUUUU	2234	1395-1417
AD-1948652	ACGCCUGGGCAC UCACGGUAU	754	1409-1429	ATACCGTGAGUGC CCAGGCGUAA	2235	1407-1429
AD-1948653	CACUGCCUCUUC ACAGAGCUU	755	1433-1453	AAGCTCTGUGAAG AGGCAGUGGG	2236	1431-1453
AD-1948654	CACUGCCUCUUC ACAGAGCUU	756	1433-1453	AAGCTCTGUGAAG AGGCAGUGGG	2237	1431-1453
AD-1948655	CUGCCACAAACA UGGCUAUCU	757	1453-1473	AGAUAGCCAUGT UUGUGGCAGAG	2238	1451-1473
AD-1948656	UGCCACAAACAU GGCUAUCCU	758	1454-1474	AGGATAGCCAUG UUUGUGGCAGA	2239	1452-1474

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948657	GCCACAAACAUG GCUAUCCAU	759	1455-1475	ATGGAUAGCCATG UUUGUGGCAG	2240	1453-1475
AD-1948658	GCCACAAACAUG GCUAUCCAU	760	1455-1475	AUGGAUAGCCAU GUUUGUGGCAG	2241	1453-1475
AD-1948659	CCACAAACAUGG CUAUCCACU	761	1456-1476	AGUGGATAGCCA UGUUUGUGGCA	2242	1454-1476
AD-1948660	CCACAAACAUGG CUAUCCACU	762	1456-1476	AGUGGATAGCCA UGUUUGUGGCA	2243	1454-1476
AD-1948661	CACAAACAUGGC UAUCCACCU	763	1457-1477	AGGUGGAUAGCC AUGUUUGUGGC	2244	1455-1477
AD-1948662	CACAAACAUGGC UAUCCACCU	764	1457-1477	AGGUGGAUAGCC AUGUUUGUGGC	2245	1455-1477
AD-1948663	UCCACCGGUCCC AGCCAUGGU	765	1471-1491	ACCATGGCUGGG ACCGGUGGAUA	2246	1469-1491
AD-1948664	CCACCGGUCCCA GCCAUGGUU	766	1472-1492	AACCAUGGCUGG GACCGGUGGAU	2247	1470-1492
AD-1948665	CACCGGUCCCAG CCAUGGUUU	767	1473-1493	AAACCATGGCUG GGACCGGUGGA	2248	1471-1493
AD-1948666	CACCGGUCCCAG CCAUGGUUU	768	1473-1493	AAACCATGGCUG GGACCGGUGGA	2249	1471-1493
AD-1948667	CCGGUCCCAGCC AUGGUUUCU	769	1475-1495	AGAAACCAUGGC UGGGACCGGUG	2250	1473-1495
AD-1948668	GUCCCAGCCAUG GUUUCACCU	770	1478-1498	AGGUGAAACCAT GGCUGGGACCG	2251	1476-1498
AD-1948669	GUCCCAGCCAUG GUUUCACCU	771	1478-1498	AGGUGAAACCAU GGCUGGGACCG	2252	1476-1498
AD-1948670	UCCCAGCCAUGG UUUCACCAU	772	1479-1499	ATGGTGAAACCAU GGCUGGGACC	2253	1477-1499
AD-1948671	UCCCAGCCAUGG UUUCACCAU	773	1479-1499	AUGGTGAAACCA UGGCUGGGACC	2254	1477-1499
AD-1948672	CCCAGCCAUGGU UUCACCACU	774	1480-1500	AGUGGUGAAACC AUGGCUGGGAC	2255	1478-1500
AD-1948673	CCAGCCAUGGUU UCACCACAU	775	1481-1501	ATGUGGTGAAACC AUGGCUGGGA	2256	1479-1501
AD-1948674	CCAGCCAUGGUU UCACCACAU	776	1481-1501	AUGUGGTGAAAC CAUGGCUGGGA	2257	1479-1501
AD-1948675	CAGCCAUGGUUU CACCACAAU	777	1482-1502	ATUGTGGUGAAA CCAUGGCUGGG	2258	1480-1502
AD-1948676	AGCCAUGGUUUC ACCACAAAU	778	1483-1503	ATUUGUGGUGAA ACCAUGGCUGG	2259	1481-1503
AD-1948677	GCCAUGGUUUCA CCACAAAAU	779	1484-1504	ATUUTGTGGUGAA ACCAUGGCUG	2260	1482-1504
AD-1948678	GCCAUGGUUUCA CCACAAAAU	780	1484-1504	AUUUTGTGGUGA AACCAUGGCUG	2261	1482-1504
AD-1948679	CCAUGGUUUCAC CACAAAAUU	781	1485-1505	AAUUTUGUGGUG AAACCAUGGCU	2262	1483-1505
AD-1948680	CAUGGUUUCACC ACAAAAUUU	782	1486-1506	AAAUTUTGUGGTG AAACCAUGGC	2263	1484-1506

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948681	AUGGUUUCACCACAAAAUUUU	783	1487-1507	AAAATUTUGUGGUGAAACCAUGG	2264	1485-1507
AD-1948682	UGGUUUCACCACAAAAUUUCU	784	1488-1508	AGAAAUTUUGUGGUGAAACCAUG	2265	1486-1508
AD-1948683	GGUUUCACCACAAAAUUUCUU	785	1489-1509	AAGAAATUUUGTGGUGAAACCAU	2266	1487-1509
AD-1948684	GUUUCACCACAAAAUUUCUAU	786	1490-1510	ATAGAAAUUUUGUGGUGAAACCA	2267	1488-1510
AD-1948685	UUUCACCACAAAAUUUCUAGU	787	1491-1511	ACUAGAAAUUUTGUGGUGAAACC	2268	1489-1511
AD-1948686	UUCACCACAAAAUUUCUAGAU	788	1492-1512	ATCUAGAAAUUTUGUGGUGAAAC	2269	1490-1512
AD-1948687	UCACCACAAAAUUUCUAGAGU	789	1493-1513	ACUCTAGAAAUTUUGUGGUGAAA	2270	1491-1513
AD-1948688	CACCACAAAAUUUCUAGAGAU	790	1494-1514	ATCUCUAGAAATUUUGUGGUGAA	2271	1492-1514
AD-1948689	CACCACAAAAUUUCUAGAGAU	791	1494-1514	AUCUCUAGAAAUUUUGUGGUGAA	2272	1492-1514
AD-1948690	ACCACAAAAUUUCUAGAGAUU	792	1495-1515	AAUCTCTAGAAAUUUUGUGGUGA	2273	1493-1515
AD-1948691	ACCACAAAAUUUCUAGAGAUU	793	1495-1515	AAUCTCTAGAAAUUUUGUGGUGA	2274	1493-1515
AD-1948692	CCACAAAAUUUCUAGAGAUGU	794	1496-1516	ACAUCUCUAGAAAUUUUGUGGUG	2275	1494-1516
AD-1948693	CACAAAAUUUCUAGAGAUGAU	795	1497-1517	ATCATCTCUAGAAAUUUUGUGGU	2276	1495-1517
AD-1948694	CACAAAAUUUCUAGAGAUGAU	796	1497-1517	AUCATCTCUAGAAAUUUUGUGGU	2277	1495-1517
AD-1948695	ACAAAAUUUCUAGAGAUGAGU	797	1498-1518	ACUCAUCUCUAGAAAUUUUGUGG	2278	1496-1518
AD-1948696	CAAAAUUUCUAGAGAUGAGGU	798	1499-1519	ACCUCATCUCUAGAAAUUUUGUG	2279	1497-1519
AD-1948697	AAAAUUUCUAGAGAUGAGGCU	799	1500-1520	AGCCTCAUCUCTAGAAAUUUUGU	2280	1498-1520
AD-1948698	AAAAUUUCUAGAGAUGAGGCU	800	1500-1520	AGCCTCAUCUCUAGAAAUUUUGU	2281	1498-1520
AD-1948699	AAAUUUCUAGAGAUGAGGCUU	801	1501-1521	AAGCCUCAUCUCUAGAAAUUUUG	2282	1499-1521
AD-1948700	AAUUUCUAGAGAUGAGGCUCU	802	1502-1522	AGAGCCTCAUCTCUAGAAAUUUU	2283	1500-1522
AD-1948701	AAUUUCUAGAGAUGAGGCUCU	803	1502-1522	AGAGCCTCAUCUCUAGAAAUUUU	2284	1500-1522
AD-1948702	AUUUCUAGAGAUGAGGCUCAU	804	1503-1523	ATGAGCCUCAUCUCUAGAAAUUU	2285	1501-1523
AD-1948703	UAGAGAUGAGGCUCAGCGAUU	805	1508-1528	AAUCGCTGAGCCUCAUCUCUAGA	2286	1506-1528
AD-1948704	AGAGAUGAGGCUCAGCGAUUU	806	1509-1529	AAAUCGCUGAGCCUCAUCUCUAG	2287	1507-1529

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948705	GAUGAGGCUCAG CGAUUGAUU	807	1512-1532	AAUCAATCGCUG AGCCUCAUCUC	2288	1510-1532
AD-1948706	GAUGAGGCUCAG CGAUUGAUU	808	1512-1532	AAUCAATCGCUG AGCCUCAUCUC	2289	1510-1532
AD-1948707	AUGAGGCUCAGC GAUUGAUUU	809	1513-1533	AAAUCAAUCGCT GAGCCUCAUCU	2290	1511-1533
AD-1948708	UGAGGCUCAGCG AUUGAUUAU	810	1514-1534	ATAATCAAUCGCU GAGCCUCAUC	2291	1512-1534
AD-1948709	UGAGGCUCAGCG AUUGAUUAU	811	1514-1534	AUAATCAAUCGC UGAGCCUCAUC	2292	1512-1534
AD-1948710	GAGGCUCAGCGA UUGAUUAUU	812	1515-1535	AAUAAUCAAUCG CUGAGCCUCAU	2293	1513-1535
AD-1948711	AGGCUCAGCGAU UGAUUAUUU	813	1516-1536	AAAUAATCAAUC GCUGAGCCUCA	2294	1514-1536
AD-1948712	GGCUCAGCGAUU GAUUAUUCU	814	1517-1537	AGAATAAUCAATC GCUGAGCCUC	2295	1515-1537
AD-1948713	GCUCAGCGAUUG AUUAUUCAU	815	1518-1538	ATGAAUAAUCAA UCGCUGAGCCU	2296	1516-1538
AD-1948714	CUCAGCGAUUGA UUAUUCAGU	816	1519-1539	ACUGAATAAUCA AUCGCUGAGCC	2297	1517-1539
AD-1948715	UCAGCGAUUGAU UAUUCAGCU	817	1520-1540	AGCUGAAUAAUC AAUCGCUGAGC	2298	1518-1540
AD-1948716	UCAGCGAUUGAU UAUUCAGCU	818	1520-1540	AGCUGAAUAAUC AAUCGCUGAGC	2299	1518-1540
AD-1948717	CAGCGAUUGAUU AUUCAGCAU	819	1521-1541	ATGCTGAAUAATC AAUCGCUGAG	2300	1519-1541
AD-1948718	CAGCGAUUGAUU AUUCAGCAU	820	1521-1541	AUGCTGAAUAAU CAAUCGCUGAG	2301	1519-1541
AD-1948719	AGCGAUUGAUUA UUCAGCAAU	821	1522-1542	ATUGCUGAAUAA UCAAUCGCUGA	2302	1520-1542
AD-1948720	GCGAUUGAUUAU UCAGCAAGU	822	1523-1543	ACUUGCTGAAUA AUCAAUCGCUG	2303	1521-1543
AD-1948721	GCGAUUGAUUAU UCAGCAAGU	823	1523-1543	ACUUGCTGAAUA AUCAAUCGCUG	2304	1521-1543
AD-1948722	CGAUUGAUUAUU CAGCAAGGU	824	1524-1544	ACCUTGCUGAATA AUCAAUCGCU	2305	1522-1544
AD-1948723	GAUUGAUUAUUC AGCAAGGAU	825	1525-1545	ATCCTUGCUGAAU AAUCAAUCGC	2306	1523-1545
AD-1948724	AUUGAUUAUUCA GCAAGGACU	826	1526-1546	AGUCCUTGCUGA AUAAUCAAUCG	2307	1524-1546
AD-1948725	AUUGAUUAUUCA GCAAGGACU	827	1526-1546	AGUCCUTGCUGA AUAAUCAAUCG	2308	1524-1546
AD-1948726	UUGAUUAUUCAG CAAGGACUU	828	1527-1547	AAGUCCTUGCUG AAUAAUCAAUC	2309	1525-1547
AD-1948727	UUGAUUAUUCAG CAAGGACUU	829	1527-1547	AAGUCCTUGCUG AAUAAUCAAUC	2310	1525-1547
AD-1948728	UGAUUAUUCAGC AAGGACUUU	830	1528-1548	AAAGTCCUUGCTG AAUAAUCAAU	2311	1526-1548

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948729	GAUUAUUCAGCAAGGACUUGU	831	1529-1549	ACAAGUCCUUGCUGAAUAAUCAA	2312	1527-1549
AD-1948730	AUUAUUCAGCAAGGACUUGUU	832	1530-1550	AACAAGTCCUUGCUGAAUAAUCA	2313	1528-1550
AD-1948731	AUUAUUCAGCAAGGACUUGUU	833	1530-1550	AACAAGTCCUUGCUGAAUAAUCA	2314	1528-1550
AD-1948732	UUAUUCAGCAAGGACUUGUGU	834	1531-1551	ACACAAGUCCUTGCUGAAUAAUC	2315	1529-1551
AD-1948733	UAUUCAGCAAGGACUUGUGGU	835	1532-1552	ACCACAAGUCCTUGCUGAAUAAU	2316	1530-1552
AD-1948734	AUUCAGCAAGGACUUGUGGAU	836	1533-1553	ATCCACAAGUCCUUGCUGAAUAA	2317	1531-1553
AD-1948735	UUCAGCAAGGACUUGUGGAUU	837	1534-1554	AAUCCACAAGUCCUUGCUGAAUA	2318	1532-1554
AD-1948736	GCAAGGACUUGUGGAUGGAGU	838	1538-1558	ACUCCATCCACAAGUCCUUGCUG	2319	1536-1558
AD-1948737	CAAGGACUUGUGGAUGGAGUU	839	1539-1559	AACUCCAUCCACAAGUCCUUGCU	2320	1537-1559
AD-1948738	CAAGGACUUGUGGAUGGAGUU	840	1539-1559	AACUCCAUCCACAAGUCCUUGCU	2321	1537-1559
AD-1948739	AGGACUUGUGGAUGGAGUUUU	841	1541-1561	AAAACUCCAUCCACAAGUCCUUG	2322	1539-1561
AD-1948740	GGACUUGUGGAUGGAGUUUUU	842	1542-1562	AAAAACTCCAUCCACAAGUCCUU	2323	1540-1562
AD-1948741	GGACUUGUGGAUGGAGUUUUU	843	1542-1562	AAAAACTCCAUCCACAAGUCCUU	2324	1540-1562
AD-1948742	GACUUGUGGAUGGAGUUUUCU	844	1543-1563	AGAAAACUCCATCCACAAGUCCU	2325	1541-1563
AD-1948743	ACUUGUGGAUGGAGUUUUCUU	845	1544-1564	AAGAAAACUCCAUCCACAAGUCC	2326	1542-1564
AD-1948744	CUUGUGGAUGGAGUUUUCUUU	846	1545-1565	AAAGAAAACUCCAUCCACAAGUC	2327	1543-1565
AD-1948745	UUGUGGAUGGAGUUUUCUUGU	847	1546-1566	ACAAGAAAACUCCAUCCACAAGU	2328	1544-1566
AD-1948746	UGUGGAUGGAGUUUUCUUGGU	848	1547-1567	ACCAAGAAAACTCCAUCCACAAG	2329	1545-1567
AD-1948747	GUGGAUGGAGUUUUCUUGGUU	849	1548-1568	AACCAAGAAAACUCCAUCCACAA	2330	1546-1568
AD-1948748	UGGAUGGAGUUUUCUUGGUAU	850	1549-1569	ATACCAAGAAAACUCCAUCCACA	2331	1547-1569
AD-1948749	UGGAUGGAGUUUUCUUGGUAU	851	1549-1569	AUACCAAGAAAACUCCAUCCACA	2332	1547-1569
AD-1948750	GGAUGGAGUUUUCUUGGUACU	852	1550-1570	AGUACCAAGAAAACUCCAUCCAC	2333	1548-1570
AD-1948751	GAUGGAGUUUUCUUGGUACGU	853	1551-1571	ACGUACCAAGAAAACUCCAUCCA	2334	1549-1571
AD-1948752	AUGGAGUUUUCUUGGUACGGU	854	1552-1572	ACCGTACCAAGAAAACUCCAUCC	2335	1550-1572

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948753	UGGAGUUUUCUUGGUACGGGU	855	1553-1573	ACCCGUACCAAGAAAACUCCAUC	2336	1551-1573
AD-1948754	GAGUUUUCUUGGUACGGGAUU	856	1555-1575	AAUCCCGUACCAAGAAAACUCCA	2337	1553-1575
AD-1948755	AGUUUUCUUGGUACGGGAUAU	857	1556-1576	ATAUCCCGUACCAAGAAAACUCC	2338	1554-1576
AD-1948756	GUUUUCUUGGUACGGGAUAGU	858	1557-1577	ACUATCCCGUACCAAGAAAACUC	2339	1555-1577
AD-1948757	UUUUCUUGGUACGGGAUAGUU	859	1558-1578	AACUAUCCCGUACCAAGAAAACU	2340	1556-1578
AD-1948758	UUUCUUGGUACGGGAUAGUCU	860	1559-1579	AGACTATCCCGTACCAAGAAAAC	2341	1557-1579
AD-1948759	UUUCUUGGUACGGGAUAGUCU	861	1559-1579	AGACTATCCCGUACCAAGAAAAC	2342	1557-1579
AD-1948760	UUCUUGGUACGGGAUAGUCAU	862	1560-1580	ATGACUAUCCCGUACCAAGAAAA	2343	1558-1580
AD-1948761	UUCUUGGUACGGGAUAGUCAU	863	1560-1580	AUGACUAUCCCGUACCAAGAAAA	2344	1558-1580
AD-1948762	UCUUGGUACGGGAUAGUCAGU	864	1561-1581	ACUGACTAUCCCGUACCAAGAAA	2345	1559-1581
AD-1948763	UCUUGGUACGGGAUAGUCAGU	865	1561-1581	ACUGACTAUCCCGUACCAAGAAA	2346	1559-1581
AD-1948764	CUUGGUACGGGAUAGUCAGAU	866	1562-1582	ATCUGACUAUCCCGUACCAAGAA	2347	1560-1582
AD-1948765	UUGGUACGGGAUAGUCAGAGU	867	1563-1583	ACUCTGACUAUCCCGUACCAAGA	2348	1561-1583
AD-1948766	UUGGUACGGGAUAGUCAGAGU	868	1563-1583	ACUCTGACUAUCCCGUACCAAGA	2349	1561-1583
AD-1948767	UGGUACGGGAUAGUCAGAGUU	869	1564-1584	AACUCUGACUATCCCGUACCAAG	2350	1562-1584
AD-1948768	GGUACGGGAUAGUCAGAGUAU	870	1565-1585	ATACTCTGACUAUCCCGUACCAA	2351	1563-1585
AD-1948769	GGUACGGGAUAGUCAGAGUAU	871	1565-1585	AUACTCTGACUAUCCCGUACCAA	2352	1563-1585
AD-1948770	GUACGGGAUAGUCAGAGUAAU	872	1566-1586	ATUACUCUGACTAUCCCGUACCA	2353	1564-1586
AD-1948771	UACGGGAUAGUCAGAGUAACU	873	1567-1587	AGUUACTCUGACUAUCCCGUACC	2354	1565-1587
AD-1948772	UACGGGAUAGUCAGAGUAACU	874	1567-1587	AGUUACTCUGACUAUCCCGUACC	2355	1565-1587
AD-1948773	ACGGGAUAGUCAGAGUAACCU	875	1568-1588	AGGUTACUCUGACUAUCCCGUAC	2356	1566-1588
AD-1948774	CAAAACUUUCGUACUGUCAAU	876	1589-1609	ATUGACAGUACGAAAGUUUUGGG	2357	1587-1609
AD-1948775	CAAAACUUUCGUACUGUCAAU	877	1589-1609	AUUGACAGUACGAAAGUUUUGGG	2358	1587-1609
AD-1948776	AAAACUUUCGUACUGUCAAUU	878	1590-1610	AAUUGACAGUACGAAAGUUUUGG	2359	1588-1610

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948777	AAACUUUCGUAC UGUCAAUGU	879	1591-1611	ACAUTGACAGUA CGAAAGUUUUG	2360	1589-1611
AD-1948778	AAACUUUCGUAC UGUCAAUGU	880	1591-1611	ACAUTGACAGUA CGAAAGUUUUG	2361	1589-1611
AD-1948779	AACUUUCGUACU GUCAAUGAU	881	1592-1612	ATCATUGACAGTA CGAAAGUUUU	2362	1590-1612
AD-1948780	ACUUUCGUACUG UCAAUGAGU	882	1593-1613	ACUCAUTGACAG UACGAAAGUUU	2363	1591-1613
AD-1948781	CUUUCGUACUGU CAAUGAGUU	883	1594-1614	AACUCATUGACA GUACGAAAGUU	2364	1592-1614
AD-1948782	CUUUCGUACUGU CAAUGAGUU	884	1594-1614	AACUCATUGACA GUACGAAAGUU	2365	1592-1614
AD-1948783	UUUCGUACUGUC AAUGAGUCU	885	1595-1615	AGACTCAUUGAC AGUACGAAAGU	2366	1593-1615
AD-1948784	UUUCGUACUGUC AAUGAGUCU	886	1595-1615	AGACTCAUUGAC AGUACGAAAGU	2367	1593-1615
AD-1948785	UUCGUACUGUCA AUGAGUCAU	887	1596-1616	ATGACUCAUUGA CAGUACGAAAG	2368	1594-1616
AD-1948786	UCGUACUGUCAA UGAGUCAUU	888	1597-1617	AAUGACTCAUUG ACAGUACGAAA	2369	1595-1617
AD-1948787	UCGUACUGUCAA UGAGUCAUU	889	1597-1617	AAUGACTCAUUG ACAGUACGAAA	2370	1595-1617
AD-1948788	CGUACUGUCAAU GAGUCAUGU	890	1598-1618	ACAUGACUCAUT GACAGUACGAA	2371	1596-1618
AD-1948789	GUACUGUCAAUG AGUCAUGGU	891	1599-1619	ACCATGACUCATU GACAGUACGA	2372	1597-1619
AD-1948790	GUACUGUCAAUG AGUCAUGGU	892	1599-1619	ACCATGACUCAUU GACAGUACGA	2373	1597-1619
AD-1948791	UACUGUCAAUGA GUCAUGGAU	893	1600-1620	ATCCAUGACUCAU UGACAGUACG	2374	1598-1620
AD-1948792	ACUGUCAAUGAG UCAUGGACU	894	1601-1621	AGUCCATGACUCA UUGACAGUAC	2375	1599-1621
AD-1948793	ACUGUCAAUGAG UCAUGGACU	895	1601-1621	AGUCCATGACUCA UUGACAGUAC	2376	1599-1621
AD-1948794	CUGUCAAUGAGU CAUGGACAU	896	1602-1622	ATGUCCAUGACTC AUUGACAGUA	2377	1600-1622
AD-1948795	CUGUCAAUGAGU CAUGGACAU	897	1602-1622	AUGUCCAUGACU CAUUGACAGUA	2378	1600-1622
AD-1948796	UGUCAAUGAGUC AUGGACAAU	898	1603-1623	ATUGTCCAUGACU CAUUGACAGU	2379	1601-1623
AD-1948797	GUCAAUGAGUCA UGGACAAAU	899	1604-1624	ATUUGUCCAUGA CUCAUUGACAG	2380	1602-1624
AD-1948798	UCAAUGAGUCAU GGACAAAAU	900	1605-1625	ATUUTGTCCAUGA CUCAUUGACA	2381	1603-1625
AD-1948799	UCAAUGAGUCAU GGACAAAAU	901	1605-1625	AUUUTGTCCAUGA CUCAUUGACA	2382	1603-1625
AD-1948800	CAAUGAGUCAUG GACAAAAAU	902	1606-1626	ATUUTUGUCCATG ACUCAUUGAC	2383	1604-1626

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948801	AAUGAGUCAUGGACAAAAAAU	903	1607-1627	ATUUTUTGUCCAUGACUCAUUGA	2384	1605-1627
AD-1948802	AAUGAGUCAUGGACAAAAAAU	904	1607-1627	AUUUTUTGUCCAUGACUCAUUGA	2385	1605-1627
AD-1948803	AUGAGUCAUGGACAAAAAAUU	905	1608-1628	AAUUTUTUGUCCAUGACUCAUUG	2386	1606-1628
AD-1948804	AUGAGUCAUGGACAAAAAAUU	906	1608-1628	AAUUTUTUGUCCAUGACUCAUUG	2387	1606-1628
AD-1948805	UGAGUCAUGGACAAAAAAUAU	907	1609-1629	ATAUTUTUUGUCCAUGACUCAUU	2388	1607-1629
AD-1948806	UGAGUCAUGGACAAAAAAUAU	908	1609-1629	AUAUTUTUUGUCCAUGACUCAUU	2389	1607-1629
AD-1948807	GAGUCAUGGACAAAAAAUAAU	909	1610-1630	ATUATUTUUUGTCCAUGACUCAU	2390	1608-1630
AD-1948808	GAGUCAUGGACAAAAAAUAAU	910	1610-1630	AUUATUTUUUGUCCAUGACUCAU	2391	1608-1630
AD-1948809	AGUCAUGGACAAAAAAUAAAU	911	1611-1631	ATUUAUTUUUUGUCCAUGACUCA	2392	1609-1631
AD-1948810	AGUCAUGGACAAAAAAUAAAU	912	1611-1631	AUUUAUTUUUUGUCCAUGACUCA	2393	1609-1631
AD-1948811	GUCAUGGACAAAAAAUAAAGU	913	1612-1632	ACUUTATUUUUTGUCCAUGACUC	2394	1610-1632
AD-1948812	UCAUGGACAAAAAAUAAAGCU	914	1613-1633	AGCUTUAUUUUTUGUCCAUGACU	2395	1611-1633
AD-1948813	CAUGGACAAAAAAUAAAGCAU	915	1614-1634	ATGCTUTAUUUTUUGUCCAUGAC	2396	1612-1634
AD-1948814	CAUGGACAAAAAAUAAAGCAU	916	1614-1634	AUGCTUTAUUUUUUGUCCAUGAC	2397	1612-1634
AD-1948815	AUGGACAAAAAAUAAAGCACU	917	1615-1635	AGUGCUTUAUUTUUUGUCCAUGA	2398	1613-1635
AD-1948816	AUGGACAAAAAAUAAAGCACU	918	1615-1635	AGUGCUTUAUUUUUUGUCCAUGA	2399	1613-1635
AD-1948817	UGGACAAAAAAUAAAGCACUU	919	1616-1636	AAGUGCTUUAUTUUUUGUCCAUG	2400	1614-1636
AD-1948818	UGGACAAAAAAUAAAGCACUU	920	1616-1636	AAGUGCTUUAUUUUUUGUCCAUG	2401	1614-1636
AD-1948819	GGACAAAAAAUAAAGCACUUU	921	1617-1637	AAAGTGCUUUATUUUUUGUCCAU	2402	1615-1637
AD-1948820	GACAAAAAAUAAAGCACUUUU	922	1618-1638	AAAAGUGCUUUAUUUUUUGUCCA	2403	1616-1638
AD-1948821	ACAAAAAAUAAAGCACUUUCU	923	1619-1639	AGAAAGTGCUUTAUUUUUUGUCC	2404	1617-1639
AD-1948822	ACAAAAAAUAAAGCACUUUCU	924	1619-1639	AGAAAGTGCUUUAUUUUUUGUCC	2405	1617-1639
AD-1948823	CAAAAAAUAAAGCACUUUCAU	925	1620-1640	ATGAAAGUGCUTUAUUUUUUGUC	2406	1618-1640
AD-1948824	AAAGCACUUUCAAAUUAUACU	926	1628-1648	AGUATAAUUUGAAAGUGCUUUAU	2407	1626-1648

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948825	AAGCACUUUCAAAUUAUACCU	927	1629-1649	AGGUAUAAUUUGAAAGUGCUUUA	2408	1627-1649
AD-1948826	AGCACUUUCAAAUUAUACCAU	928	1630-1650	ATGGTATAAUUTGAAAGUGCUUU	2409	1628-1650
AD-1948827	AGCACUUUCAAAUUAUACCAU	929	1630-1650	AUGGTATAAUUUGAAAGUGCUUU	2410	1628-1650
AD-1948828	GCACUUUCAAAUUAUACCAGU	930	1631-1651	ACUGGUAUAAUTUGAAAGUGCUU	2411	1629-1651
AD-1948829	CACUUUCAAAUUAUACCAGUU	931	1632-1652	AACUGGTAUAATUUGAAAGUGCU	2412	1630-1652
AD-1948830	CACUUUCAAAUUAUACCAGUU	932	1632-1652	AACUGGTAUAAUUUGAAAGUGCU	2413	1630-1652
AD-1948831	ACUUUCAAAUUAUACCAGUAU	933	1633-1653	ATACTGGUAUAAUUUGAAAGUGC	2414	1631-1653
AD-1948832	CUUUCAAAUUAUACCAGUAGU	934	1634-1654	ACUACUGGUAUAAUUUGAAAGUG	2415	1632-1654
AD-1948833	UUUCAAAUUAUACCAGUAGAU	935	1635-1655	ATCUACTGGUATAAUUUGAAAGU	2416	1633-1655
AD-1948834	UUUCAAAUUAUACCAGUAGAU	936	1635-1655	AUCUACTGGUAUAAUUUGAAAGU	2417	1633-1655
AD-1948835	UUCAAAUUAUACCAGUAGAAU	937	1636-1656	ATUCTACUGGUAUAAUUUGAAAG	2418	1634-1656
AD-1948836	UCAAAUUAUACCAGUAGAAGU	938	1637-1657	ACUUCUACUGGTAUAAUUUGAAA	2419	1635-1657
AD-1948837	CAAAUUAUACCAGUAGAAGAU	939	1638-1658	ATCUTCTACUGGUAUAAUUUGAA	2420	1636-1658
AD-1948838	CAAAUUAUACCAGUAGAAGAU	940	1638-1658	AUCUTCTACUGGUAUAAUUUGAA	2421	1636-1658
AD-1948839	AAAUUAUACCAGUAGAAGAUU	941	1639-1659	AAUCTUCUACUGGUAUAAUUUGA	2422	1637-1659
AD-1948840	AAUUAUACCAGUAGAAGAUGU	942	1640-1660	ACAUCUTCUACTGGUAUAAUUUG	2423	1638-1660
AD-1948841	AUUAUACCAGUAGAAGAUGAU	943	1641-1661	ATCATCTUCUACUGGUAUAAUUU	2424	1639-1661
AD-1948842	AUUAUACCAGUAGAAGAUGAU	944	1641-1661	AUCATCTUCUACUGGUAUAAUUU	2425	1639-1661
AD-1948843	UUAUACCAGUAGAAGAUGACU	945	1642-1662	AGUCAUCUUCUACUGGUAUAAUU	2426	1640-1662
AD-1948844	UAUACCAGUAGAAGAUGACGU	946	1643-1663	ACGUCATCUUCTACUGGUAUAAU	2427	1641-1663
AD-1948845	UAUACCAGUAGAAGAUGACGU	947	1643-1663	ACGUCATCUUCUACUGGUAUAAU	2428	1641-1663
AD-1948846	UACCAGUAGAAGAUGACGGUU	948	1645-1665	AACCGUCAUCUTCUACUGGUAUA	2429	1643-1665
AD-1948847	ACCAGUAGAAGAUGACGGUGU	949	1646-1666	ACACCGTCAUCTUCUACUGGUAU	2430	1644-1666
AD-1948848	CCAGUAGAAGAUGACGGUGAU	950	1647-1667	ATCACCGUCAUCUUCUACUGGUA	2431	1645-1667

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948849	CAGUAGAAGAUGACGGUGAAU	951	1648-1668	ATUCACCGUCATCUUCUACUGGU	2432	1646-1668
AD-1948850	AGUAGAAGAUGACGGUGAAAU	952	1649-1669	ATUUCACCGUCAUCUUCUACUGG	2433	1647-1669
AD-1948851	GUAGAAGAUGACGGUGAAAUU	953	1650-1670	AAUUTCACCGUCAUCUUCUACUG	2434	1648-1670
AD-1948852	GUAGAAGAUGACGGUGAAAUU	954	1650-1670	AAUUTCACCGUCAUCUUCUACUG	2435	1648-1670
AD-1948853	UAGAAGAUGACGGUGAAAUGU	955	1651-1671	ACAUTUCACCGTCAUCUUCUACU	2436	1649-1671
AD-1948854	AGAAGAUGACGGUGAAAUGUU	956	1652-1672	AACATUTCACCGUCAUCUUCUAC	2437	1650-1672
AD-1948855	AGAAGAUGACGGUGAAAUGUU	957	1652-1672	AACATUTCACCGUCAUCUUCUAC	2438	1650-1672
AD-1948856	GAAGAUGACGGUGAAAUGUUU	958	1653-1673	AAACAUTUCACCGUCAUCUUCUA	2439	1651-1673
AD-1948857	AAGAUGACGGUGAAAUGUUCU	959	1654-1674	AGAACATUUCACCGUCAUCUUCU	2440	1652-1674
AD-1948858	AAGAUGACGGUGAAAUGUUCU	960	1654-1674	AGAACATUUCACCGUCAUCUUCU	2441	1652-1674
AD-1948859	AGAUGACGGUGAAAUGUUCCU	961	1655-1675	AGGAACAUUUCACCGUCAUCUUC	2442	1653-1675
AD-1948860	AGAUGACGGUGAAAUGUUCCU	962	1655-1675	AGGAACAUUUCACCGUCAUCUUC	2443	1653-1675
AD-1948861	GAUGACGGUGAAAUGUUCCAU	963	1656-1676	ATGGAACAUUUCACCGUCAUCUU	2444	1654-1676
AD-1948862	AUGACGGUGAAAUGUUCCACU	964	1657-1677	AGUGGAACAUUTCACCGUCAUCU	2445	1655-1677
AD-1948863	AUGACGGUGAAAUGUUCCACU	965	1657-1677	AGUGGAACAUUUCACCGUCAUCU	2446	1655-1677
AD-1948864	UGACGGUGAAAUGUUCCACAU	966	1658-1678	ATGUGGAACAUTUCACCGUCAUC	2447	1656-1678
AD-1948865	UGACGGUGAAAUGUUCCACAU	967	1658-1678	AUGUGGAACAUUUCACCGUCAUC	2448	1656-1678
AD-1948866	GACGGUGAAAUGUUCCACACU	968	1659-1679	AGUGTGGAACATUUCACCGUCAU	2449	1657-1679
AD-1948867	ACGGUGAAAUGUUCCACACAU	969	1660-1680	ATGUGUGGAACAUUUCACCGUCA	2450	1658-1680
AD-1948868	CGGUGAAAUGUUCCACACACU	970	1661-1681	AGUGTGTGGAACAUUUCACCGUC	2451	1659-1681
AD-1948869	CGGUGAAAUGUUCCACACACU	971	1661-1681	AGUGTGTGGAACAUUUCACCGUC	2452	1659-1681
AD-1948870	GGUGAAAUGUUCCACACACUU	972	1662-1682	AAGUGUGUGGAACAUUUCACCGU	2453	1660-1682
AD-1948871	GUGAAAUGUUCCACACACUGU	973	1663-1683	ACAGTGTGUGGAACAUUUCACCG	2454	1661-1683
AD-1948872	GUGAAAUGUUCCACACACUGU	974	1663-1683	ACAGTGTGUGGAACAUUUCACCG	2455	1661-1683

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948873	GAAAUGUUCCAC ACACUGGAU	975	1665-1685	ATCCAGTGUGUGG AACAUUUCAC	2456	1663-1685
AD-1948874	GAAAUGUUCCAC ACACUGGAU	976	1665-1685	AUCCAGTGUGUG GAACAUUUCAC	2457	1663-1685
AD-1948875	AAAUGUUCCACA CACUGGAUU	977	1666-1686	AAUCCAGUGUGT GGAACAUUUCA	2458	1664-1686
AD-1948876	AAUGUUCCACAC ACUGGAUGU	978	1667-1687	ACAUCCAGUGUG UGGAACAUUUC	2459	1665-1687
AD-1948877	AUGUUCCACACA CUGGAUGAU	979	1668-1688	ATCATCCAGUGTG UGGAACAUUU	2460	1666-1688
AD-1948878	UGUUCCACACAC UGGAUGAUU	980	1669-1689	AAUCAUCCAGUG UGUGGAACAUU	2461	1667-1689
AD-1948879	GUUCCACACACU GGAUGAUGU	981	1670-1690	ACAUCATCCAGTG UGUGGAACAU	2462	1668-1690
AD-1948880	CCACACAAGAUU UACAGAUCU	982	1691-1711	AGAUCUGUAAAT CUUGUGUGGCC	2463	1689-1711
AD-1948881	CACACAAGAUUU ACAGAUCUU	983	1692-1712	AAGATCTGUAAA UCUUGUGUGGC	2464	1690-1712
AD-1948882	CACACAAGAUUU ACAGAUCUU	984	1692-1712	AAGATCTGUAAA UCUUGUGUGGC	2465	1690-1712
AD-1948883	ACACAAGAUUUA CAGAUCUAU	985	1693-1713	ATAGAUCUGUAA AUCUUGUGUGG	2466	1691-1713
AD-1948884	CACAAGAUUUAC AGAUCUAAU	986	1694-1714	ATUAGATCUGUA AAUCUUGUGUG	2467	1692-1714
AD-1948885	CACAAGAUUUAC AGAUCUAAU	987	1694-1714	AUUAGATCUGUA AAUCUUGUGUG	2468	1692-1714
AD-1948886	ACAAGAUUUACA GAUCUAAUU	988	1695-1715	AAUUAGAUCUGT AAAUCUUGUGU	2469	1693-1715
AD-1948887	ACAAGAUUUACA GAUCUAAUU	989	1695-1715	AAUUAGAUCUGU AAAUCUUGUGU	2470	1693-1715
AD-1948888	CAAGAUUUACAG AUCUAAUAU	990	1696-1716	ATAUTAGAUCUG UAAAUCUUGUG	2471	1694-1716
AD-1948889	AAGAUUUACAGA UCUAAUACU	991	1697-1717	AGUATUAGAUCT GUAAAUCUUGU	2472	1695-1717
AD-1948890	AAGAUUUACAGA UCUAAUACU	992	1697-1717	AGUATUAGAUCU GUAAAUCUUGU	2473	1695-1717
AD-1948891	AGAUUUACAGAU CUAAUACAU	993	1698-1718	ATGUAUTAGAUC UGUAAAUCUUG	2474	1696-1718
AD-1948892	AGAUUUACAGAU CUAAUACAU	994	1698-1718	AUGUAUTAGAUC UGUAAAUCUUG	2475	1696-1718
AD-1948893	AGCUGGUGGAGU UCUAUCAAU	995	1717-1737	ATUGAUAGAACTC CACCAGCUGU	2476	1715-1737
AD-1948894	AGCUGGUGGAGU UCUAUCAAU	996	1717-1737	AUUGAUAGAACU CCACCAGCUGU	2477	1715-1737
AD-1948895	GCUGGUGGAGUU CUAUCAACU	997	1718-1738	AGUUGATAGAAC UCCACCAGCUG	2478	1716-1738
AD-1948896	GCUGGUGGAGUU CUAUCAACU	998	1718-1738	AGUUGATAGAAC UCCACCAGCUG	2479	1716-1738

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948897	CUGGUGGAGUUCUAUCAACUU	999	1719-1739	AAGUTGAUAGAACUCCACCAGCU	2480	1717-1739
AD-1948898	CUGGUGGAGUUCUAUCAACUU	1000	1719-1739	AAGUTGAUAGAACUCCACCAGCU	2481	1717-1739
AD-1948899	UGGUGGAGUUCUAUCAACUCU	1001	1720-1740	AGAGTUGAUAGAACUCCACCAGC	2482	1718-1740
AD-1948900	GGUGGAGUUCUAUCAACUCAU	1002	1721-1741	ATGAGUTGAUAGAACUCCACCAG	2483	1719-1741
AD-1948901	GGUGGAGUUCUAUCAACUCAU	1003	1721-1741	AUGAGUTGAUAGAACUCCACCAG	2484	1719-1741
AD-1948902	GUGGAGUUCUAUCAACUCAAU	1004	1722-1742	ATUGAGTUGAUAGAACUCCACCA	2485	1720-1742
AD-1948903	GUGGAGUUCUAUCAACUCAAU	1005	1722-1742	AUUGAGTUGAUAGAACUCCACCA	2486	1720-1742
AD-1948904	UGGAGUUCUAUCAACUCAAUU	1006	1723-1743	AAUUGAGUUGATAGAACUCCACC	2487	1721-1743
AD-1948905	GGAGUUCUAUCAACUCAAUAU	1007	1724-1744	ATAUTGAGUUGAUAGAACUCCAC	2488	1722-1744
AD-1948906	GGAGUUCUAUCAACUCAAUAU	1008	1724-1744	AUAUTGAGUUGAUAGAACUCCAC	2489	1722-1744
AD-1948907	GAGUUCUAUCAACUCAAUAAU	1009	1725-1745	ATUATUGAGUUGAUAGAACUCCA	2490	1723-1745
AD-1948908	AGUUCUAUCAACUCAAUAAGU	1010	1726-1746	ACUUAUTGAGUTGAUAGAACUCC	2491	1724-1746
AD-1948909	GUUCUAUCAACUCAAUAAGGU	1011	1727-1747	ACCUTATUGAGTUGAUAGAACUC	2492	1725-1747
AD-1948910	UUCUAUCAACUCAAUAAGGGU	1012	1728-1748	ACCCTUAUUGAGUUGAUAGAACU	2493	1726-1748
AD-1948911	UCUAUCAACUCAAUAAGGGCU	1013	1729-1749	AGCCCUTAUUGAGUUGAUAGAAC	2494	1727-1749
AD-1948912	UAUCAACUCAAUAAGGGCGUU	1014	1731-1751	AACGCCCUUAUTGAGUUGAUAGA	2495	1729-1751
AD-1948913	AUCAACUCAAUAAGGGCGUUU	1015	1732-1752	AAACGCCCUUATUGAGUUGAUAG	2496	1730-1752
AD-1948914	UCAACUCAAUAAGGGCGUUCU	1016	1733-1753	AGAACGCCCUUAUUGAGUUGAUA	2497	1731-1753
AD-1948915	CAACUCAAUAAGGGCGUUCUU	1017	1734-1754	AAGAACGCCCUTAUUGAGUUGAU	2498	1732-1754
AD-1948916	AACUCAAUAAGGGCGUUCUUU	1018	1735-1755	AAAGAACGCCCTUAUUGAGUUGA	2499	1733-1755
AD-1948917	ACUCAAUAAGGGCGUUCUUCU	1019	1736-1756	AGAAGAACGCCCUUAUUGAGUUG	2500	1734-1756
AD-1948918	ACUCAAUAAGGGCGUUCUUCU	1020	1736-1756	AGAAGAACGCCCUUAUUGAGUUG	2501	1734-1756
AD-1948919	CUCAAUAAGGGCGUUCUUCCU	1021	1737-1757	AGGAAGAACGCCCUUAUUGAGUU	2502	1735-1757
AD-1948920	UCAAUAAGGGCGUUCUUCCUU	1022	1738-1758	AAGGAAGAACGCCCUUAUUGAGU	2503	1736-1758

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948921	CAAUAAGGGCGUUCUUCCUUU	1023	1739-1759	AAAGGAAGAACGCCCUUAUUGAG	2504	1737-1759
AD-1948922	CAAUAAGGGCGUUCUUCCUUU	1024	1739-1759	AAAGGAAGAACGCCCUUAUUGAG	2505	1737-1759
AD-1948923	AAUAAGGGCGUUCUUCCUUGU	1025	1740-1760	ACAAGGAAGAACGCCCUUAUUGA	2506	1738-1760
AD-1948924	AAGGGCGUUCUUCCUUGCAAU	1026	1743-1763	ATUGCAAGGAAGAACGCCCUUAU	2507	1741-1763
AD-1948925	AAGGGCGUUCUUCCUUGCAAU	1027	1743-1763	AUUGCAAGGAAGAACGCCCUUAU	2508	1741-1763
AD-1948926	GGCGUUCUUCCUUGCAAGUUU	1028	1746-1766	AAACTUGCAAGGAAGAACGCCCU	2509	1744-1766
AD-1948927	GCGUUCUUCCUUGCAAGUUGU	1029	1747-1767	ACAACUTGCAAGGAAGAACGCCC	2510	1745-1767
AD-1948928	CGUUCUUCCUUGCAAGUUGAU	1030	1748-1768	ATCAACTUGCAAGGAAGAACGCC	2511	1746-1768
AD-1948929	CGUUCUUCCUUGCAAGUUGAU	1031	1748-1768	AUCAACTUGCAAGGAAGAACGCC	2512	1746-1768
AD-1948930	GUUCUUCCUUGCAAGUUGAAU	1032	1749-1769	ATUCAACUUGCAAGGAAGAACGC	2513	1747-1769
AD-1948931	UUCUUCCUUGCAAGUUGAAAU	1033	1750-1770	ATUUCAACUUGCAAGGAAGAACG	2514	1748-1770
AD-1948932	UUCUUCCUUGCAAGUUGAAAU	1034	1750-1770	AUUUCAACUUGCAAGGAAGAACG	2515	1748-1770
AD-1948933	UCUUCCUUGCAAGUUGAAACU	1035	1751-1771	AGUUTCAACUUGCAAGGAAGAAC	2516	1749-1771
AD-1948934	UCUUCCUUGCAAGUUGAAACU	1036	1751-1771	AGUUTCAACUUGCAAGGAAGAAC	2517	1749-1771
AD-1948935	CUUCCUUGCAAGUUGAAACAU	1037	1752-1772	ATGUTUCAACUTGCAAGGAAGAA	2518	1750-1772
AD-1948936	UUCCUUGCAAGUUGAAACAUU	1038	1753-1773	AAUGTUTCAACTUGCAAGGAAGA	2519	1751-1773
AD-1948937	UUCCUUGCAAGUUGAAACAUU	1039	1753-1773	AAUGTUTCAACUUGCAAGGAAGA	2520	1751-1773
AD-1948938	UCCUUGCAAGUUGAAACAUUU	1040	1754-1774	AAAUGUTUCAACUUGCAAGGAAG	2521	1752-1774
AD-1948939	UCCUUGCAAGUUGAAACAUUU	1041	1754-1774	AAAUGUTUCAACUUGCAAGGAAG	2522	1752-1774
AD-1948940	CCUUGCAAGUUGAAACAUUAU	1042	1755-1775	ATAATGTUUCAACUUGCAAGGAA	2523	1753-1775
AD-1948941	CCUUGCAAGUUGAAACAUUAU	1043	1755-1775	AUAATGTUUCAACUUGCAAGGAA	2524	1753-1775
AD-1948942	CUUGCAAGUUGAAACAUUAUU	1044	1756-1776	AAUAAUGUUUCAACUUGCAAGGA	2525	1754-1776
AD-1948943	UUGCAAGUUGAAACAUUAUUU	1045	1757-1777	AAAUAATGUUUCAACUUGCAAGG	2526	1755-1777
AD-1948944	UGCAAGUUGAAACAUUAUUGU	1046	1758-1778	ACAATAAUGUUTCAACUUGCAAG	2527	1756-1778

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948945	GCAAGUUGAAAC AUUAUUGUU	1047	1759-1779	AACAAUAAUGUT UCAACUUGCAA	2528	1757-1779
AD-1948946	CAAGUUGAAACA UUAUUGUGU	1048	1760-1780	ACACAATAAUGTU UCAACUUGCA	2529	1758-1780
AD-1948947	AAGUUGAAACAU UAUUGUGCU	1049	1761-1781	AGCACAAUAAUG UUUCAACUUGC	2530	1759-1781
AD-1948948	AGUUGAAACAUU AUUGUGCUU	1050	1762-1782	AAGCACAAUAAT GUUUCAACUUG	2531	1760-1782
AD-1948949	GUUGAAACAUUA UUGUGCUAU	1051	1763-1783	ATAGCACAAUAA UGUUUCAACUU	2532	1761-1783
AD-1948950	UUGAAACAUUAU UGUGCUAGU	1052	1764-1784	ACUAGCACAAUA AUGUUUCAACU	2533	1762-1784
AD-1948951	UUGAAACAUUAU UGUGCUAGU	1053	1764-1784	ACUAGCACAAUA AUGUUUCAACU	2534	1762-1784
AD-1948952	UGAAACAUUAUU GUGCUAGGU	1054	1765-1785	ACCUAGCACAATA AUGUUUCAAC	2535	1763-1785
AD-1948953	AAACAUUAUUGU GCUAGGAUU	1055	1767-1787	AAUCCUAGCACA AUAAUGUUUCA	2536	1765-1787
AD-1948954	AAACAUUAUUGU GCUAGGAUU	1056	1767-1787	AAUCCUAGCACA AUAAUGUUUCA	2537	1765-1787
AD-1948955	AACAUUAUUGUG CUAGGAUUU	1057	1768-1788	AAAUCCTAGCACA AUAAUGUUUC	2538	1766-1788
AD-1948956	AACAUUAUUGUG CUAGGAUUU	1058	1768-1788	AAAUCCTAGCACA AUAAUGUUUC	2539	1766-1788
AD-1948957	ACAUUAUUGUGC UAGGAUUGU	1059	1769-1789	ACAATCCUAGCAC AAUAAUGUUU	2540	1767-1789
AD-1948958	CAUUAUUGUGCU AGGAUUGCU	1060	1770-1790	AGCAAUCCUAGC ACAAUAAUGUU	2541	1768-1790
AD-1948959	AUUAUUGUGCUA GGAUUGCUU	1061	1771-1791	AAGCAATCCUAGC ACAAUAAUGU	2542	1769-1791
AD-1948960	UUAUUGUGCUAG GAUUGCUCU	1062	1772-1792	AGAGCAAUCCUA GCACAAUAAUG	2543	1770-1792
AD-1948961	UUAUUGUGCUAG GAUUGCUCU	1063	1772-1792	AGAGCAAUCCUA GCACAAUAAUG	2544	1770-1792
AD-1948962	UAUUGUGCUAGG AUUGCUCUU	1064	1773-1793	AAGAGCAAUCCT AGCACAAUAAU	2545	1771-1793
AD-1948963	UAUUGUGCUAGG AUUGCUCUU	1065	1773-1793	AAGAGCAAUCCU AGCACAAUAAU	2546	1771-1793
AD-1948964	AUUGUGCUAGGA UUGCUCUCU	1066	1774-1794	AGAGAGCAAUCC UAGCACAAUAA	2547	1772-1794
AD-1948965	UUGUGCUAGGAU UGCUCUCUU	1067	1775-1795	AAGAGAGCAAUC CUAGCACAAUA	2548	1773-1795
AD-1948966	UGUGCUAGGAUU GCUCUCUAU	1068	1776-1796	ATAGAGAGCAATC CUAGCACAAU	2549	1774-1796
AD-1948967	UGUGCUAGGAUU GCUCUCUAU	1069	1776-1796	AUAGAGAGCAAU CCUAGCACAAU	2550	1774-1796
AD-1948968	GUGCUAGGAUUG CUCUCUAGU	1070	1777-1797	ACUAGAGAGCAA UCCUAGCACAA	2551	1775-1797

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948969	AGCCAGAAGUGACUUAUUAAU	1071	1800-1820	ATUAAUAAGUCACUUCUGGCUUG	2552	1798-1820
AD-1948970	GCCAGAAGUGACUUAUUAAAU	1072	1801-1821	ATUUAATAAGUCACUUCUGGCUU	2553	1799-1821
AD-1948971	CCAGAAGUGACUUAUUAAACU	1073	1802-1822	AGUUTAAUAAGTCACUUCUGGCU	2554	1800-1822
AD-1948972	CAGAAGUGACUUAUUAAACUU	1074	1803-1823	AAGUTUAAUAAGUCACUUCUGGC	2555	1801-1823
AD-1948973	AGAAGUGACUUAUUAAACUAU	1075	1804-1824	ATAGTUTAAUAAGUCACUUCUGG	2556	1802-1824
AD-1948974	AGAAGUGACUUAUUAAACUAU	1076	1804-1824	AUAGTUTAAUAAGUCACUUCUGG	2557	1802-1824
AD-1948975	GAAGUGACUUAUUAAACUAUU	1077	1805-1825	AAUAGUTUAAUAAGUCACUUCUG	2558	1803-1825
AD-1948976	GAAGUGACUUAUUAAACUAUU	1078	1805-1825	AAUAGUTUAAUAAGUCACUUCUG	2559	1803-1825
AD-1948977	AAGUGACUUAUUAAACUAUUU	1079	1806-1826	AAAUAGTUUAATAAGUCACUUCU	2560	1804-1826
AD-1948978	AAGUGACUUAUUAAACUAUUU	1080	1806-1826	AAAUAGTUUAAUAAGUCACUUCU	2561	1804-1826
AD-1948979	AGUGACUUAUUAAACUAUUGU	1081	1807-1827	ACAATAGUUUAAUAAGUCACUUC	2562	1805-1827
AD-1948980	UGACUUAUUAAACUAUUGAAU	1082	1809-1829	ATUCAATAGUUTAAUAAGUCACU	2563	1807-1829
AD-1948981	GACUUAUUAAACUAUUGAAGU	1083	1810-1830	ACUUCAAUAGUTUAAUAAGUCAC	2564	1808-1830
AD-1948982	GGAAAAGGACUCAAGAAAAAU	1084	1829-1849	ATUUTUCUUGAGUCCUUUUCCUU	2565	1827-1849
AD-1948983	GAAAAGGACUCAAGAAAAAUU	1085	1830-1850	AAUUTUTCUUGAGUCCUUUUCCU	2566	1828-1850
AD-1948984	GAAAAGGACUCAAGAAAAAUU	1086	1830-1850	AAUUTUTCUUGAGUCCUUUUCCU	2567	1828-1850
AD-1948985	AAAAGGACUCAAGAAAAAUAU	1087	1831-1851	ATAUTUTUCUUGAGUCCUUUUCC	2568	1829-1851
AD-1948986	AAAAGGACUCAAGAAAAAUAU	1088	1831-1851	AUAUTUTUCUUGAGUCCUUUUCC	2569	1829-1851
AD-1948987	AAAGGACUCAAGAAAAAUAAU	1089	1832-1852	ATUATUTUUCUTGAGUCCUUUUC	2570	1830-1852
AD-1948988	AAAGGACUCAAGAAAAAUAAU	1090	1832-1852	AUUATUTUUCUUGAGUCCUUUUC	2571	1830-1852
AD-1948989	ACUCAAGAAAAAUAAUAAAAU	1091	1837-1857	ATUUTATUAUUTUUCUUGAGUCC	2572	1835-1857
AD-1948990	ACUCAAGAAAAAUAAUAAAAU	1092	1837-1857	AUUUTATUAUUUUUCUUGAGUCC	2573	1835-1857
AD-1948991	CAAGAAAAAUAAUAAAAGACU	1093	1840-1860	AGUCTUTUAUUAUUUUUCUUGAG	2574	1838-1860
AD-1948992	CAAGAAAAAUAAUAAAAGACU	1094	1840-1860	AGUCTUTUAUUAUUUUUCUUGAG	2575	1838-1860

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1948993	AUAAAAGACCAUAAAUAAGGU	1095	1851-1871	ACCUTATUUAUGGUCUUUUAUUA	2576	1849-1871
AD-1948994	UAAAAGACCAUAAAUAAGGGU	1096	1852-1872	ACCCTUAUUUATGGUCUUUUAUU	2577	1850-1872
AD-1948995	ACCAUGUGAAAAGAAUGUAUU	1097	1882-1902	AAUACATUCUUTUCACAUGGUAA	2578	1880-1902
AD-1948996	CCAUGUGAAAAGAAUGUAUUU	1098	1883-1903	AAAUACAUUCUTUUCACAUGGUA	2579	1881-1903
AD-1948997	CCAUGUGAAAAGAAUGUAUUU	1099	1883-1903	AAAUACAUUCUUUUCACAUGGUA	2580	1881-1903
AD-1948998	CAUGUGAAAAGAAUGUAUUUU	1100	1884-1904	AAAATACAUUCTUUUCACAUGGU	2581	1882-1904
AD-1948999	UCACCUGCAAGUUACAAAAAU	1101	1903-1923	ATUUTUGUAACTUGCAGGUGAAA	2582	1901-1923
AD-1949000	CACCUGCAAGUUACAAAAAAU	1102	1904-1924	ATUUTUTGUAACUUGCAGGUGAA	2583	1902-1924
AD-1949001	CACCUGCAAGUUACAAAAAAU	1103	1904-1924	AUUUTUTGUAACUUGCAGGUGAA	2584	1902-1924
AD-1949002	ACCUGCAAGUUACAAAAAAU	1104	1905-1925	ATUUTUTUGUAACUUGCAGGUGA	2585	1903-1925
AD-1949003	ACCUGCAAGUUACAAAAAAU	1105	1905-1925	AUUUTUTUGUAACUUGCAGGUGA	2586	1903-1925
AD-1949004	AAAAAAAUAGUUUGUGCAUUU	1106	1918-1938	AAAUGCACAAACUAUUUUUUUGU	2587	1916-1938
AD-1949005	AAAAAAAUAGUUUGUGCAUUU	1107	1918-1938	AAAUGCACAAACUAUUUUUUUGU	2588	1916-1938
AD-1949006	UGCAAAUAAGCAAAGACUUGU	1108	1937-1957	ACAAGUCUUUGCUUAUUUGCAAU	2589	1935-1957
AD-1949007	GCAAAUAAGCAAAGACUUGGU	1109	1938-1958	ACCAAGTCUUUGCUUAUUUGCAA	2590	1936-1958
AD-1949008	CAAAUAAGCAAAGACUUGGAU	1110	1939-1959	ATCCAAGUCUUTGCUUAUUUGCA	2591	1937-1959
AD-1949009	AAAUAAGCAAAGACUUGGAUU	1111	1940-1960	AAUCCAAGUCUTUGCUUAUUUGC	2592	1938-1960
AD-1949010	AAAUAAGCAAAGACUUGGAUU	1112	1940-1960	AAUCCAAGUCUUUGCUUAUUUGC	2593	1938-1960
AD-1949011	AAUAAGCAAAGACUUGGAUUU	1113	1941-1961	AAAUCCAAGUCTUUGCUUAUUUG	2594	1939-1961
AD-1949012	AUAAGCAAAGACUUGGAUUGU	1114	1942-1962	ACAATCCAAGUCUUUGCUUAUUU	2595	1940-1962
AD-1949013	UAAGCAAAGACUUGGAUUGAU	1115	1943-1963	ATCAAUCCAAGTCUUUGCUUAUU	2596	1941-1963
AD-1949014	AAGCAAAGACUUGGAUUGACU	1116	1944-1964	AGUCAATCCAAGUCUUUGCUUAU	2597	1942-1964
AD-1949015	AAGCAAAGACUUGGAUUGACU	1117	1944-1964	AGUCAATCCAAGUCUUUGCUUAU	2598	1942-1964
AD-1949016	AGCAAAGACUUGGAUUGACUU	1118	1945-1965	AAGUCAAUCCAAGUCUUUGCUUA	2599	1943-1965

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-1949017	AGCAAAGACUUGGAUUGACUU	1119	1945-1965	AAGUCAAUCCAAGUCUUUGCUUA	2600	1943-1965
AD-1949018	GCAAAGACUUGGAUUGACUUU	1120	1946-1966	AAAGTCAAUCCAAGUCUUUGCUU	2601	1944-1966
AD-1949019	GCAAAGACUUGGAUUGACUUU	1121	1946-1966	AAAGTCAAUCCAAGUCUUUGCUU	2602	1944-1966
AD-1949020	CAAAGACUUGGAUUGACUUUU	1122	1947-1967	AAAAGUCAAUCCAAGUCUUUGCU	2603	1945-1967
AD-1949021	AAAGACUUGGAUUGACUUUAU	1123	1948-1968	ATAAAGTCAAUCCAAGUCUUUGC	2604	1946-1968
AD-1949022	AAAGACUUGGAUUGACUUUAU	1124	1948-1968	AUAAAGTCAAUCCAAGUCUUUGC	2605	1946-1968
AD-1949023	AAGACUUGGAUUGACUUUACU	1125	1949-1969	AGUAAAGUCAATCCAAGUCUUUG	2606	1947-1969
AD-1949024	AGACUUGGAUUGACUUUACAU	1126	1950-1970	ATGUAAAGUCAAUCCAAGUCUUU	2607	1948-1970
AD-1949025	AGACUUGGAUUGACUUUACAU	1127	1950-1970	AUGUAAAGUCAAUCCAAGUCUUU	2608	1948-1970
AD-1949026	GACUUGGAUUGACUUUACAUU	1128	1951-1971	AAUGTAAAGUCAAUCCAAGUCUU	2609	1949-1971
AD-1949027	ACUUGGAUUGACUUUACAUUU	1129	1952-1972	AAAUGUAAAGUCAAUCCAAGUCU	2610	1950-1972
AD-1949028	CUUGGAUUGACUUUACAUUCU	1130	1953-1973	AGAATGTAAAGTCAAUCCAAGUC	2611	1951-1973
AD-1949029	CUUGGAUUGACUUUACAUUCU	1131	1953-1973	AGAATGTAAAGUCAAUCCAAGUC	2612	1951-1973
AD-1949030	UUGGAUUGACUUUACAUUCAU	1132	1954-1974	ATGAAUGUAAAGUCAAUCCAAGU	2613	1952-1974
AD-1949031	UGGAUUGACUUUACAUUCAUU	1133	1955-1975	AAUGAATGUAAAGUCAAUCCAAG	2614	1953-1975
AD-1949032	GGAUUGACUUUACAUUCAUCU	1134	1956-1976	AGAUGAAUGUAAAGUCAAUCCAA	2615	1954-1976
AD-1949033	GGAUUGACUUUACAUUCAUCU	1135	1956-1976	AGAUGAAUGUAAAGUCAAUCCAA	2616	1954-1976
AD-1949034	GAUUGACUUUACAUUCAUCAU	1136	1957-1977	ATGATGAAUGUAAAGUCAAUCCA	2617	1955-1977
AD-1949035	GAUUGACUUUACAUUCAUCAU	1137	1957-1977	AUGATGAAUGUAAAGUCAAUCCA	2618	1955-1977
AD-1949036	AUUGACUUUACAUUCAUCAUU	1138	1958-1978	AAUGAUGAAUGTAAAGUCAAUCC	2619	1956-1978
AD-1949037	UUGACUUUACAUUCAUCAUUU	1139	1959-1979	AAAUGATGAAUGUAAAGUCAAUC	2620	1957-1979
AD-1949038	UUGACUUUACAUUCAUCAUUU	1140	1959-1979	AAAUGATGAAUGUAAAGUCAAUC	2621	1957-1979
AD-2017365.1	GUGUUGUCAGCAGACCUAUUU	1141	450-470	AAAUAGGUCUGCUGACAACACAG	2622	448-470
AD-2017366.1	UGUUGUCAGCAGACCUAUUUU	1142	451-471	AAAATAGGUCUGCUGACAACACA	2623	449-471

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017367.1	GUUGUCAGCAGACCUAUUUCU	1143	452-472	AGAAAUAGGUCTGCUGACAACAC	2624	450-472
AD-2017368.1	UUGUCAGCAGACCUAUUUCCU	1144	453-473	AGGAAATAGGUCUGCUGACAACA	2625	451-473
AD-2017369.1	UGUCAGCAGACCUAUUUCCCU	1145	454-474	AGGGAAAUAGGTCUGCUGACAAC	2626	452-474
AD-2017370.1	GUCAGCAGACCUAUUUCCCAU	1146	455-475	ATGGGAAAUAGGUCUGCUGACAA	2627	453-475
AD-2017371.1	UCAGCAGACCUAUUUCCCAAU	1147	456-476	ATUGGGAAAUAGGUCUGCUGACA	2628	454-476
AD-2017372.1	CAGCAGACCUAUUUCCCAAAU	1148	457-477	ATUUGGGAAAUAGGUCUGCUGAC	2629	455-477
AD-2017373.1	AGCAGACCUAUUUCCCAAAGU	1149	458-478	ACUUTGGGAAATAGGUCUGCUGA	2630	456-478
AD-2017374.1	GCAGACCUAUUUCCCAAAGCU	1150	459-479	AGCUTUGGGAAAUAGGUCUGCUG	2631	457-479
AD-2017375.1	CAGACCUAUUUCCCAAAGCAU	1151	460-480	ATGCTUTGGGAAAUAGGUCUGCU	2632	458-480
AD-2017376.1	AGACCUAUUUCCCAAAGCAAU	1152	461-481	ATUGCUTUGGGAAAUAGGUCUGC	2633	459-481
AD-2017377.1	GACCUAUUUCCCAAAGCAAAU	1153	462-482	ATUUGCTUUGGGAAAUAGGUCUG	2634	460-482
AD-2017378.1	ACCUAUUUCCCAAAGCAAAUU	1154	463-483	AAUUTGCUUUGGGAAAUAGGUCU	2635	461-483
AD-2017379.1	CCUAUUUCCCAAAGCAAAUUU	1155	464-484	AAAUTUGCUUUGGGAAAUAGGUC	2636	462-484
AD-2017380.1	CUAUUUCCCAAAGCAAAUUCU	1156	465-485	AGAATUTGCUUTGGGAAAUAGGU	2637	463-485
AD-2017381.1	AAAAACAGGUGAUUAAAGUAU	1157	490-510	ATACTUTAAUCACCUGUUUUUUC	2638	488-510
AD-2017382.1	AAACAGGUGAUUAAAGUAUAU	1158	492-512	ATAUACTUUAATCACCUGUUUUU	2639	490-512
AD-2017383.1	AACAGGUGAUUAAAGUAUACU	1159	493-513	AGUATACUUUAAUCACCUGUUUU	2640	491-513
AD-2017384.1	ACAGGUGAUUAAAGUAUACAU	1160	494-514	ATGUAUACUUUAAUCACCUGUUU	2641	492-514
AD-2017385.1	CAGGUGAUUAAAGUAUACAGU	1161	495-515	ACUGTATACUUTAAUCACCUGUU	2642	493-515
AD-2017386.1	AGGUGAUUAAAGUAUACAGUU	1162	496-516	AACUGUAUACUTUAAUCACCUGU	2643	494-516
AD-2017387.1	GGUGAUUAAAGUAUACAGUGU	1163	497-517	ACACTGTAUACTUUAAUCACCUG	2644	495-517
AD-2017388.1	GUGAUUAAAGUAUACAGUGAU	1164	498-518	ATCACUGUAUACUUUAAUCACCU	2645	496-518
AD-2017389.1	UGAUUAAAGUAUACAGUGAAU	1165	499-519	ATUCACTGUAUACUUUAAUCACC	2646	497-519
AD-2017390.1	GAUUAAAGUAUACAGUGAAGU	1166	500-520	ACUUCACUGUATACUUUAAUCAC	2647	498-520

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017391.1	AUUAAAGUAUAC AGUGAAGAU	1167	501-521	ATCUTCACUGUAU ACUUUAAUCA	2648	499-521
AD-2017392.1	UUAAAGUAUACA GUGAAGAUU	1168	502-522	AAUCTUCACUGTA UACUUUAAUC	2649	500-522
AD-2017393.1	UAAAGUAUACAG UGAAGAUGU	1169	503-523	ACAUCUTCACUGU AUACUUUAAU	2650	501-523
AD-2017394.1	AAAGUAUACAGU GAAGAUGAU	1170	504-524	ATCATCTUCACTG UAUACUUUAA	2651	502-524
AD-2017395.1	AAGUAUACAGUG AAGAUGAAU	1171	505-525	ATUCAUCUUCACU GUAUACUUUA	2652	503-525
AD-2017396.1	AGUAUACAGUGA AGAUGAAAU	1172	506-526	ATUUCATCUUCAC UGUAUACUUU	2653	504-526
AD-2017397.1	GUAUACAGUGAA GAUGAAACU	1173	507-527	AGUUTCAUCUUC ACUGUAUACUU	2654	505-527
AD-2017398.1	ACAGUGAAGAUG AAACCAGCU	1174	511-531	AGCUGGTUUCATC UUCACUGUAU	2655	509-531
AD-2017399.1	CAGUGAAGAUGA AACCAGCAU	1175	512-532	ATGCTGGUUUCAU CUUCACUGUA	2656	510-532
AD-2017400.1	AGUGAAGAUGA AACCAGCAGU	1176	513-533	ACUGCUGGUUUC AUCUUCACUGU	2657	511-533
AD-2017401.1	GUGAAGAUGAA ACCAGCAGGU	1177	514-534	ACCUGCTGGUUTC AUCUUCACUG	2658	512-534
AD-2017402.1	UGAAGAUGAAAC CAGCAGGGU	1178	515-535	ACCCTGCUGGUTU CAUCUUCACU	2659	513-535
AD-2017403.1	GAAGAUGAAACC AGCAGGGCU	1179	516-536	AGCCCUGCUGGTU UCAUCUUCAC	2660	514-536
AD-2017404.1	AAGAUGAAACCA GCAGGGCUU	1180	517-537	AAGCCCTGCUGGU UUCAUCUUCA	2661	515-537
AD-2017405.1	AGAUGAAACCAG CAGGGCUUU	1181	518-538	AAAGCCCUGCUG GUUUCAUCUUC	2662	516-538
AD-2017406.1	GAUGAAACCAGC AGGGCUUUU	1182	519-539	AAAAGCCCUGCTG GUUUCAUCUU	2663	517-539
AD-2017407.1	AUGAAACCAGCA GGGCUUUAU	1183	520-540	ATAAAGCCCUGCU GGUUUCAUCU	2664	518-540
AD-2017408.1	UGAAACCAGCAG GGCUUUAGU	1184	521-541	ACUAAAGCCCUG CUGGUUUCAUC	2665	519-541
AD-2017409.1	GAAACCAGCAGG GCUUUAGAU	1185	522-542	ATCUAAAGCCCTG CUGGUUUCAU	2666	520-542
AD-2017410.1	AAACCAGCAGGG CUUUAGAUU	1186	523-543	AAUCTAAAGCCCU GCUGGUUUCA	2667	521-543
AD-2017411.1	AACCAGCAGGGC UUUAGAUGU	1187	524-544	ACAUCUAAAGCC CUGCUGGUUUC	2668	522-544
AD-2017412.1	ACCAGCAGGGCU UUAGAUGUU	1188	525-545	AACATCTAAAGCC CUGCUGGUUU	2669	523-545
AD-2017413.1	CCAGCAGGGCUU UAGAUGUAU	1189	526-546	ATACAUCUAAAG CCCUGCUGGUU	2670	524-546
AD-2017414.1	CAGCAGGGCUUU AGAUGUACU	1190	527-547	AGUACATCUAAA GCCCUGCUGGU	2671	525-547

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017415.1	AGCAGGGCUUUA GAUGUACCU	1191	528-548	AGGUACAUCUAA AGCCCUGCUGG	2672	526-548
AD-2017416.1	AAAGAACAAUAG AAGACCACU	1192	655-675	AGUGGUCUUCUA UUGUUCUUUCU	2673	653-675
AD-2017417.1	AAGAACAAUAGA AGACCACGU	1193	656-676	ACGUGGTCUUCTA UUGUUCUUUC	2674	654-676
AD-2017418.1	AGAACAAUAGAA GACCACGAU	1194	657-677	ATCGTGGUCUUCU AUUGUUCUUU	2675	655-677
AD-2017419.1	GAACAAUAGAAG ACCACGAAU	1195	658-678	ATUCGUGGUCUTC UAUUGUUCUU	2676	656-678
AD-2017420.1	AACAAUAGAAGA CCACGAACU	1196	659-679	AGUUCGTGGUCTU CUAUUGUUCU	2677	657-679
AD-2017421.1	ACAAUAGAAGAC CACGAACUU	1197	660-680	AAGUTCGUGGUC UUCUAUUGUUC	2678	658-680
AD-2017422.1	CAAUAGAAGACC ACGAACUGU	1198	661-681	ACAGTUCGUGGTC UUCUAUUGUU	2679	659-681
AD-2017423.1	AAUAGAAGACCA CGAACUGGU	1199	662-682	ACCAGUTCGUGG UCUUCUAUUGU	2680	660-682
AD-2017424.1	AUAGAAGACCAC GAACUGGUU	1200	663-683	AACCAGTUCGUG GUCUUCUAUUG	2681	661-683
AD-2017425.1	UAGAAGACCACG AACUGGUGU	1201	664-684	ACACCAGUUCGTG GUCUUCUAUU	2682	662-684
AD-2017426.1	AGAAGACCACGA ACUGGUGAU	1202	665-685	ATCACCAGUUCGU GGUCUUCUAU	2683	663-685
AD-2017427.1	GAAGACCACGAA CUGGUGAUU	1203	666-686	AAUCACCAGUUC GUGGUCUUCUA	2684	664-686
AD-2017428.1	AAGACCACGAAC UGGUGAUUU	1204	667-687	AAAUCACCAGUTC GUGGUCUUCU	2685	665-687
AD-2017429.1	AGACCACGAACU GGUGAUUGU	1205	668-688	ACAATCACCAGTU CGUGGUCUUC	2686	666-688
AD-2017430.1	GACCACGAACUG GUGAUUGAU	1206	669-689	ATCAAUCACCAGU UCGUGGUCUU	2687	667-689
AD-2017431.1	ACCACGAACUGG UGAUUGAAU	1207	670-690	ATUCAATCACCAG UUCGUGGUCU	2688	668-690
AD-2017432.1	CCACGAACUGGU GAUUGAAGU	1208	671-691	ACUUCAAUCACC AGUUCGUGGUC	2689	669-691
AD-2017433.1	CACGAACUGGUG AUUGAAGUU	1209	672-692	AACUTCAAUCACC AGUUCGUGGU	2690	670-692
AD-2017434.1	GAUAGAAGAAG AAAACAAACU	1210	707-727	AGUUTGTUUUCTU CUUCUAUCCC	2691	705-727
AD-2017435.1	AUAGAAGAAGA AAACAAACUU	1211	708-728	AAGUTUGUUUUC UUCUUCUAUCC	2692	706-728
AD-2017436.1	UAGAAGAAGAA AACAAACUAU	1212	709-729	ATAGTUTGUUUTC UUCUUCUAUC	2693	707-729
AD-2017437.1	GAAGAAGAAAAC AAACUAUAU	1213	711-731	ATAUAGTUUGUTU UCUUCUUCUA	2694	709-731
AD-2017438.1	AAGAAGAAAACA AACUAUACU	1214	712-732	AGUATAGUUUGT UUUCUUCUUCU	2695	710-732

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017439.1	AGAAGAAAACAAACUAUACUU	1215	713-733	AAGUAUAGUUUGUUUUCUUCUUC	2696	711-733
AD-2017440.1	UUCUGAGUUCAAGCACAUAUU	1216	856-876	AAUATGTGCUUGAACUCAGAAAC	2697	854-876
AD-2017441.1	UCUGAGUUCAAGCACAUAUCU	1217	857-877	AGAUAUGUGCUTGAACUCAGAAA	2698	855-877
AD-2017442.1	CUGAGUUCAAGCACAUAUCCU	1218	858-878	AGGATATGUGCTUGAACUCAGAA	2699	856-878
AD-2017443.1	UGAGUUCAAGCACAUAUCCUU	1219	859-879	AAGGAUAUGUGCUUGAACUCAGA	2700	857-879
AD-2017444.1	GAGUUCAAGCACAUAUCCUGU	1220	860-880	ACAGGATAUGUGCUUGAACUCAG	2701	858-880
AD-2017445.1	AGUUCAAGCACAUAUCCUGAU	1221	861-881	ATCAGGAUAUGTGCUUGAACUCA	2702	859-881
AD-2017446.1	GUUCAAGCACAUAUCCUGAAU	1222	862-882	ATUCAGGAUAUGUGCUUGAACUC	2703	860-882
AD-2017447.1	UUCAAGCACAUAUCCUGAAAU	1223	863-883	ATUUCAGGAUATGUGCUUGAACU	2704	861-883
AD-2017448.1	UCAAGCACAUAUCCUGAAAUU	1224	864-884	AAUUTCAGGAUAUGUGCUUGAAC	2705	862-884
AD-2017449.1	CAAGCACAUAUCCUGAAAUUU	1225	865-885	AAAUTUCAGGATAUGUGCUUGAA	2706	863-885
AD-2017450.1	AAGCACAUAUCCUGAAAUUCU	1226	866-886	AGAATUTCAGGAUAUGUGCUUGA	2707	864-886
AD-2017451.1	AGCACAUAUCCUGAAAUUCAU	1227	867-887	ATGAAUTUCAGGAUAUGUGCUUG	2708	865-887
AD-2017452.1	GCACAUAUCCUGAAAUUCAUU	1228	868-888	AAUGAATUUCAGGAUAUGUGCUU	2709	866-888
AD-2017453.1	CACAUAUCCUGAAAUUCAUGU	1229	869-889	ACAUGAAUUUCAGGAUAUGUGCU	2710	867-889
AD-2017454.1	ACAUAUCCUGAAAUUCAUGGU	1230	870-890	ACCATGAAUUUCAGGAUAUGUGC	2711	868-890
AD-2017455.1	CAUAUCCUGAAAUUCAUGGUU	1231	871-891	AACCAUGAAUUTCAGGAUAUGUG	2712	869-891
AD-2017456.1	AUAUCCUGAAAUUCAUGGUUU	1232	872-892	AAACCATGAAUTUCAGGAUAUGU	2713	870-892
AD-2017457.1	UAUCCUGAAAUUCAUGGUUUU	1233	873-893	AAAACCAUGAATUUCAGGAUAUG	2714	871-893
AD-2017458.1	UUUUUCUACUAAAGGAACAUU	1234	965-985	AAUGTUCCUUUAGUAGAAAAAUA	2715	963-985
AD-2017459.1	UUUUCUACUAAAGGAACAUCU	1235	966-986	AGAUGUTCCUUTAGUAGAAAAAU	2716	964-986
AD-2017460.1	UUUCUACUAAAGGAACAUCAU	1236	967-987	ATGATGTUCCUTUAGUAGAAAAA	2717	965-987
AD-2017461.1	UUCUACUAAAGGAACAUCAAU	1237	968-988	ATUGAUGUUCCTUUAGUAGAAAA	2718	966-988
AD-2017462.1	UCUACUAAAGGAACAUCAAAU	1238	969-989	ATUUGATGUUCCUUUAGUAGAAA	2719	967-989

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017463.1	CUACUAAAGGAACAUCAAAGU	1239	970-990	ACUUTGAUGUUCCUUUAGUAGAA	2720	968-990
AD-2017464.1	UACUAAAGGAACAUCAAAGGU	1240	971-991	ACCUTUGAUGUTCCUUUAGUAGA	2721	969-991
AD-2017465.1	ACUAAAGGAACAUCAAAGGAU	1241	972-992	ATCCTUTGAUGTUCCUUUAGUAG	2722	970-992
AD-2017466.1	CUAAAGGAACAUCAAAGGAAU	1242	973-993	ATUCCUTUGAUGUUCCUUUAGUA	2723	971-993
AD-2017467.1	UAAAGGAACAUCAAAGGAACU	1243	974-994	AGUUCCTUUGATGUUCCUUUAGU	2724	972-994
AD-2017468.1	AAAGGAACAUCAAAGGAACCU	1244	975-995	AGGUTCCUUUGAUGUUCCUUUAG	2725	973-995
AD-2017469.1	AAGGAACAUCAAAGGAACCGU	1245	976-996	ACGGTUCCUUUGAUGUUCCUUUA	2726	974-996
AD-2017470.1	AGGAACAUCAAAGGAACCGCU	1246	977-997	AGCGGUTCCUUTGAUGUUCCUUU	2727	975-997
AD-2017471.1	GGAACAUCAAAGGAACCGCGU	1247	978-998	ACGCGGTUCCUTUGAUGUUCCUU	2728	976-998
AD-2017472.1	CACUGGCAGGCAAAAAAAAAU	1248	1045-1065	ATUUTUTUUUGCCUGCCAGUGAC	2729	1043-1065
AD-2017473.1	ACUGGCAGGCAAAAAAAACU	1249	1046-1066	AGUUTUTUUUUGCCUGCCAGUGA	2730	1044-1066
AD-2017474.1	CUGGCAGGCAAAAAAAACAU	1250	1047-1067	ATGUTUTUUUUTGCCUGCCAGUG	2731	1045-1067
AD-2017475.1	UGGCAGGCAAAAAAAACAUU	1251	1048-1068	AAUGTUTUUUUTUGCCUGCCAGU	2732	1046-1068
AD-2017476.1	GGCAGGCAAAAAAAAACAUGU	1252	1049-1069	ACAUGUTUUUUTUUGCCUGCCAG	2733	1047-1069
AD-2017477.1	GCAGGCAAAAAAAAACAUGGU	1253	1050-1070	ACCATGTUUUUTUUGCCUGCCA	2734	1048-1070
AD-2017478.1	CAGGCAAAAAAAAACAUGGAU	1254	1051-1071	ATCCAUGUUUUTUUUGCCUGCC	2735	1049-1071
AD-2017479.1	AGGCAAAAAAAAACAUGGAGU	1255	1052-1072	ACUCCATGUUUTUUUUGCCUGC	2736	1050-1072
AD-2017480.1	GGCAAAAAAAAAACAUGGAGCU	1256	1053-1073	AGCUCCAUGUUTUUUUUUGCCUG	2737	1051-1073
AD-2017481.1	GCAAAAAAAAAACAUGGAGCAU	1257	1054-1074	ATGCTCCAUGUTUUUUUUGCCU	2738	1052-1074
AD-2017482.1	CAAAAAAAAAACAUGGAGCACU	1258	1055-1075	AGUGCUCCAUGTUUUUUUUUGCC	2739	1053-1075
AD-2017483.1	AAAAAAAAAACAUGGAGCACCU	1259	1056-1076	AGGUGCTCCAUGUUUUUUUUUGC	2740	1054-1076
AD-2017484.1	AAAAAAAAACAUGGAGCACCGU	1260	1057-1077	ACGGTGCUCCATGUUUUUUUUUG	2741	1055-1077
AD-2017485.1	AAAAAAACAUGGAGCACCGAU	1261	1058-1078	ATCGGUGCUCCAUGUUUUUUUUU	2742	1056-1078
AD-2017486.1	AAAAAACAUGGAGCACCGACU	1262	1059-1079	AGUCGGTGCUCCAUGUUUUUUUU	2743	1057-1079

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017487.1	AAAAACAUGGAG CACCGACUU	1263	1060-1080	AAGUCGGUGCUC CAUGUUUUUUU	2744	1058-1080
AD-2017488.1	AAAACAUGGAGC ACCGACUAU	1264	1061-1081	ATAGTCGGUGCTC CAUGUUUUUU	2745	1059-1081
AD-2017489.1	AAACAUGGAGCA CCGACUAAU	1265	1062-1082	ATUAGUCGGUGC UCCAUGUUUUU	2746	1060-1082
AD-2017490.1	CUGAAGCCCUUU CAGUUGCGU	1266	1351-1371	ACGCAACUGAAA GGGCUUCAGUG	2747	1349-1371
AD-2017491.1	UGAAGCCCUUUC AGUUGCGGU	1267	1352-1372	ACCGCAACUGAA AGGGCUUCAGU	2748	1350-1372
AD-2017492.1	GAAGCCCUUUCA GUUGCGGUU	1268	1353-1373	AACCGCAACUGA AAGGGCUUCAG	2749	1351-1373
AD-2017493.1	AAGCCCUUUCAG UUGCGGUUU	1269	1354-1374	AAACCGCAACUG AAAGGGCUUCA	2750	1352-1374
AD-2017494.1	AGCCCUUUCAGU UGCGGUUGU	1270	1355-1375	ACAACCGCAACTG AAAGGGCUUC	2751	1353-1375
AD-2017495.1	GCCCUUUCAGUU GCGGUUGAU	1271	1356-1376	ATCAACCGCAACU GAAAGGGCUU	2752	1354-1376
AD-2017496.1	CCCUUUCAGUUG CGGUUGAAU	1272	1357-1377	ATUCAACCGCAAC UGAAAGGGCU	2753	1355-1377
AD-2017497.1	CCUUUCAGUUGC GGUUGAAGU	1273	1358-1378	ACUUCAACCGCA ACUGAAAGGGC	2754	1356-1378
AD-2017498.1	CUUUCAGUUGCG GUUGAAGAU	1274	1359-1379	ATCUTCAACCGCA ACUGAAAGGG	2755	1357-1379
AD-2017499.1	UUUCAGUUGCGG UUGAAGAAU	1275	1360-1380	ATUCTUCAACCGC AACUGAAAGG	2756	1358-1380
AD-2017500.1	UUCAGUUGCGGU UGAAGAAGU	1276	1361-1381	ACUUCUTCAACCG CAACUGAAAG	2757	1359-1381
AD-2017501.1	UCAGUUGCGGUU GAAGAAGGU	1277	1362-1382	ACCUTCTUCAACC GCAACUGAAA	2758	1360-1382
AD-2017502.1	CAGUUGCGGUUG AAGAAGGAU	1278	1363-1383	ATCCTUCUUCAAC CGCAACUGAA	2759	1361-1383
AD-2017503.1	AGUUGCGGUUGA AGAAGGACU	1279	1364-1384	AGUCCUTCUUCAA CCGCAACUGA	2760	1362-1384
AD-2017504.1	GUUGCGGUUGAA GAAGGACUU	1280	1365-1385	AAGUCCTUCUUCA ACCGCAACUG	2761	1363-1385
AD-2017505.1	UUGCGGUUGAAG AAGGACUCU	1281	1366-1386	AGAGTCCUUCUTC AACCGCAACU	2762	1364-1386
AD-2017506.1	UGCGGUUGAAGA AGGACUCGU	1282	1367-1387	ACGAGUCCUUCTU CAACCGCAAC	2763	1365-1387
AD-2017507.1	GCGGUUGAAGAA GGACUCGCU	1283	1368-1388	AGCGAGTCCUUCU UCAACCGCAA	2764	1366-1388
AD-2017508.1	CGGUUGAAGAAG GACUCGCUU	1284	1369-1389	AAGCGAGUCCUTC UUCAACCGCA	2765	1367-1389
AD-2017509.1	GGUUGAAGAAG GACUCGCUUU	1285	1370-1390	AAAGCGAGUCCT UCUUCAACCGC	2766	1368-1390
AD-2017510.1	GUUGAAGAAGG ACUCGCUUGU	1286	1371-1391	ACAAGCGAGUCC UUCUUCAACCG	2767	1369-1391

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017511.1	UUGAAGAAGGAC UCGCUUGGU	1287	1372-1392	ACCAAGCGAGUC CUUCUUCAACC	2768	1370-1392
AD-2017512.1	UGAAGAAGGACU CGCUUGGAU	1288	1373-1393	ATCCAAGCGAGTC CUUCUUCAAC	2769	1371-1393
AD-2017513.1	GAAGAAGGACUC GCUUGGAGU	1289	1374-1394	ACUCCAAGCGAG UCCUUCUUCAA	2770	1372-1394
AD-2017514.1	AAGAAGGACUCG CUUGGAGGU	1290	1375-1395	ACCUCCAAGCGA GUCCUUCUUCA	2771	1373-1395
AD-2017515.1	AGAAGGACUCGC UUGGAGGAU	1291	1376-1396	ATCCTCCAAGCGA GUCCUUCUUC	2772	1374-1396
AD-2017516.1	GAAGGACUCGCU UGGAGGAAU	1292	1377-1397	ATUCCUCCAAGCG AGUCCUUCUU	2773	1375-1397
AD-2017517.1	CUGCCUCUUCAC AGAGCUCUU	1293	1435-1455	AAGAGCTCUGUG AAGAGGCAGUG	2774	1433-1455
AD-2017518.1	UGCCUCUUCACA GAGCUCUGU	1294	1436-1456	ACAGAGCUCUGT GAAGAGGCAGU	2775	1434-1456
AD-2017519.1	GCCUCUUCACAG AGCUCUGCU	1295	1437-1457	AGCAGAGCUCUG UGAAGAGGCAG	2776	1435-1457
AD-2017520.1	CCUCUUCACAGA GCUCUGCCU	1296	1438-1458	AGGCAGAGCUCT GUGAAGAGGCA	2777	1436-1458
AD-2017521.1	CUCUUCACAGAG CUCUGCCAU	1297	1439-1459	ATGGCAGAGCUC UGUGAAGAGGC	2778	1437-1459
AD-2017522.1	UCUUCACAGAGC UCUGCCACU	1298	1440-1460	AGUGGCAGAGCT CUGUGAAGAGG	2779	1438-1460
AD-2017523.1	CUUCACAGAGCU CUGCCACAU	1299	1441-1461	ATGUGGCAGAGC UCUGUGAAGAG	2780	1439-1461
AD-2017524.1	UUCACAGAGCUC UGCCACAAU	1300	1442-1462	ATUGTGGCAGAGC UCUGUGAAGA	2781	1440-1462
AD-2017525.1	UCACAGAGCUCU GCCACAAAU	1301	1443-1463	ATUUGUGGCAGA GCUCUGUGAAG	2782	1441-1463
AD-2017526.1	CACAGAGCUCUG CCACAAACU	1302	1444-1464	AGUUTGTGGCAG AGCUCUGUGAA	2783	1442-1464
AD-2017527.1	ACAGAGCUCUGC CACAAACAU	1303	1445-1465	ATGUTUGUGGCA GAGCUCUGUGA	2784	1443-1465
AD-2017528.1	CAGAGCUCUGCC ACAAACAUU	1304	1446-1466	AAUGTUTGUGGC AGAGCUCUGUG	2785	1444-1466
AD-2017529.1	AGAGCUCUGCCA CAAACAUGU	1305	1447-1467	ACAUGUTUGUGG CAGAGCUCUGU	2786	1445-1467
AD-2017530.1	GAGCUCUGCCAC AAACAUGGU	1306	1448-1468	ACCATGTUUGUGG CAGAGCUCUG	2787	1446-1468
AD-2017531.1	AGCUCUGCCACA AACAUGGCU	1307	1449-1469	AGCCAUGUUUGT GGCAGAGCUCU	2788	1447-1469
AD-2017532.1	GCUCUGCCACAA ACAUGGCUU	1308	1450-1470	AAGCCATGUUUG UGGCAGAGCUC	2789	1448-1470
AD-2017533.1	CUCUGCCACAAA CAUGGCUAU	1309	1451-1471	ATAGCCAUGUUTG UGGCAGAGCU	2790	1449-1471
AD-2017534.1	UCUGCCACAAAC AUGGCUAUU	1310	1452-1472	AAUAGCCAUGUT UGUGGCAGAGC	2791	1450-1472

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017535.1	GAUUUACAGAUC UAAUACAGU	1311	1699-1719	ACUGTATUAGATC UGUAAAUCUU	2792	1697-1719
AD-2017536.1	AUUUACAGAUCU AAUACAGCU	1312	1700-1720	AGCUGUAUUAGA UCUGUAAAUCU	2793	1698-1720
AD-2017537.1	UUUACAGAUCUA AUACAGCUU	1313	1701-1721	AAGCTGTAUUAG AUCUGUAAAUC	2794	1699-1721
AD-2017538.1	UUACAGAUCUAA UACAGCUGU	1314	1702-1722	ACAGCUGUAUUA GAUCUGUAAAU	2795	1700-1722
AD-2017539.1	UACAGAUCUAAU ACAGCUGGU	1315	1703-1723	ACCAGCTGUAUTA GAUCUGUAAA	2796	1701-1723
AD-2017540.1	ACAGAUCUAAUA CAGCUGGUU	1316	1704-1724	AACCAGCUGUAT UAGAUCUGUAA	2797	1702-1724
AD-2017541.1	CAGAUCUAAUAC AGCUGGUGU	1317	1705-1725	ACACCAGCUGUA UUAGAUCUGUA	2798	1703-1725
AD-2017542.1	AGAUCUAAUACA GCUGGUGGU	1318	1706-1726	ACCACCAGCUGTA UUAGAUCUGU	2799	1704-1726
AD-2017543.1	GAUCUAAUACAG CUGGUGGAU	1319	1707-1727	ATCCACCAGCUGU AUUAGAUCUG	2800	1705-1727
AD-2017544.1	AUCUAAUACAGC UGGUGGAGU	1320	1708-1728	ACUCCACCAGCTG UAUUAGAUCU	2801	1706-1728
AD-2017545.1	UCUAAUACAGCU GGUGGAGUU	1321	1709-1729	AACUCCACCAGCU GUAUUAGAUC	2802	1707-1729
AD-2017546.1	CUAAUACAGCUG GUGGAGUUU	1322	1710-1730	AAACTCCACCAGC UGUAUUAGAU	2803	1708-1730
AD-2017547.1	UAAUACAGCUGG UGGAGUUCU	1323	1711-1731	AGAACUCCACCA GCUGUAUUAGA	2804	1709-1731
AD-2017548.1	AAUACAGCUGGU GGAGUUCUU	1324	1712-1732	AAGAACTCCACCA GCUGUAUUAG	2805	1710-1732
AD-2017549.1	AUACAGCUGGUG GAGUUCUAU	1325	1713-1733	ATAGAACUCCACC AGCUGUAUUA	2806	1711-1733
AD-2017550.1	UACAGCUGGUGG AGUUCUAUU	1326	1714-1734	AAUAGAACUCCA CCAGCUGUAUU	2807	1712-1734
AD-2017551.1	ACAGCUGGUGGA GUUCUAUCU	1327	1715-1735	AGAUAGAACUCC ACCAGCUGUAU	2808	1713-1735
AD-2017552.1	CAGCUGGUGGAG UUCUAUCAU	1328	1716-1736	ATGATAGAACUCC ACCAGCUGUA	2809	1714-1736
AD-2017553.1	UGCUAGGAUUGC UCUCUAGAU	1329	1778-1798	ATCUAGAGAGCA AUCCUAGCACA	2810	1776-1798
AD-2017554.1	GCUAGGAUUGCU CUCUAGACU	1330	1779-1799	AGUCTAGAGAGC AAUCCUAGCAC	2811	1777-1799
AD-2017555.1	CUAGGAUUGCUC UCUAGACAU	1331	1780-1800	ATGUCUAGAGAG CAAUCCUAGCA	2812	1778-1800
AD-2017556.1	UAGGAUUGCUCU CUAGACAAU	1332	1781-1801	ATUGTCTAGAGAG CAAUCCUAGC	2813	1779-1801
AD-2017557.1	AGGAUUGCUCUC UAGACAAGU	1333	1782-1802	ACUUGUCUAGAG AGCAAUCCUAG	2814	1780-1802
AD-2017558.1	GGAUUGCUCUCU AGACAAGCU	1334	1783-1803	AGCUTGTCUAGAG AGCAAUCCUA	2815	1781-1803

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017559.1	GAUUGCUCUCUA GACAAGCCU	1335	1784-1804	AGGCTUGUCUAG AGAGCAAUCCU	2816	1782-1804
AD-2017560.1	AUUGCUCUCUAG ACAAGCCAU	1336	1785-1805	ATGGCUTGUCUAG AGAGCAAUCC	2817	1783-1805
AD-2017561.1	UUGCUCUCUAGA CAAGCCAGU	1337	1786-1806	ACUGGCTUGUCTA GAGAGCAAUC	2818	1784-1806
AD-2017562.1	UGCUCUCUAGAC AAGCCAGAU	1338	1787-1807	ATCUGGCUUGUC UAGAGAGCAAU	2819	1785-1807
AD-2017563.1	GCUCUCUAGACA AGCCAGAAU	1339	1788-1808	ATUCTGGCUUGTC UAGAGAGCAA	2820	1786-1808
AD-2017564.1	CUCUCUAGACAA GCCAGAAGU	1340	1789-1809	ACUUCUGGCUUG UCUAGAGAGCA	2821	1787-1809
AD-2017565.1	UCUCUAGACAAG CCAGAAGUU	1341	1790-1810	AACUTCTGGCUTG UCUAGAGAGC	2822	1788-1810
AD-2017566.1	CUCUAGACAAGC CAGAAGUGU	1342	1791-1811	ACACTUCUGGCTU GUCUAGAGAG	2823	1789-1811
AD-2017567.1	UCUAGACAAGCC AGAAGUGAU	1343	1792-1812	ATCACUTCUGGCU UGUCUAGAGA	2824	1790-1812
AD-2017568.1	CUAGACAAGCCA GAAGUGACU	1344	1793-1813	AGUCACTUCUGGC UUGUCUAGAG	2825	1791-1813
AD-2017569.1	UAGACAAGCCAG AAGUGACUU	1345	1794-1814	AAGUCACUUCUG GCUUGUCUAGA	2826	1792-1814
AD-2017570.1	AGACAAGCCAGA AGUGACUUU	1346	1795-1815	AAAGTCACUUCTG GCUUGUCUAG	2827	1793-1815
AD-2017571.1	GACAAGCCAGAA GUGACUUAU	1347	1796-1816	ATAAGUCACUUC UGGCUUGUCUA	2828	1794-1816
AD-2017572.1	ACAAGCCAGAAG UGACUUAUU	1348	1797-1817	AAUAAGTCACUTC UGGCUUGUCU	2829	1795-1817
AD-2017573.1	CAAGCCAGAAGU GACUUAUUU	1349	1798-1818	AAAUAAGUCACT UCUGGCUUGUC	2830	1796-1818
AD-2017574.1	AAGCCAGAAGUG ACUUAUUAU	1350	1799-1819	ATAATAAGUCACU UCUGGCUUGU	2831	1797-1819
AD-2017575.1	ACUUAUUAAACU AUUGAAGGU	1351	1811-1831	ACCUTCAAUAGTU UAAUAAGUCA	2832	1809-1831
AD-2017576.1	CUUAUUAAACUA UUGAAGGAU	1352	1812-1832	ATCCTUCAAUAGU UUAAUAAGUC	2833	1810-1832
AD-2017577.1	UUAAACUAUUGA AGGAAAAGU	1353	1816-1836	ACUUTUCCUUCAA UAGUUUAAUA	2834	1814-1836
AD-2017578.1	UAAACUAUUGAA GGAAAAGGU	1354	1817-1837	ACCUTUTCCUUCA AUAGUUUAAU	2835	1815-1837
AD-2017579.1	AAACUAUUGAAG GAAAAGGAU	1355	1818-1838	ATCCTUTUCCUTC AAUAGUUUAA	2836	1816-1838
AD-2017580.1	AACUAUUGAAGG AAAAGGACU	1356	1819-1839	AGUCCUTUUCCTU CAAUAGUUUA	2837	1817-1839
AD-2017581.1	ACUAUUGAAGGA AAAGGACUU	1357	1820-1840	AAGUCCTUUUCCU UCAAUAGUUU	2838	1818-1840
AD-2017582.1	CUAUUGAAGGAA AAGGACUCU	1358	1821-1841	AGAGTCCUUUUCC UUCAAUAGUU	2839	1819-1841

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017583.1	UAUUGAAGGAAAAGGACUCAU	1359	1822-1842	ATGAGUCCUUUTCCUUCAAUAGU	2840	1820-1842
AD-2017584.1	AUUGAAGGAAAAGGACUCAAU	1360	1823-1843	ATUGAGTCCUUTUCCUUCAAUAG	2841	1821-1843
AD-2017585.1	UUGAAGGAAAAGGACUCAAGU	1361	1824-1844	ACUUGAGUCCUTUUCCUUCAAUA	2842	1822-1844
AD-2017586.1	UGAAGGAAAAGGACUCAAGAU	1362	1825-1845	ATCUTGAGUCCTUUUCCUUCAAU	2843	1823-1845
AD-2017587.1	GAAGGAAAAGGACUCAAGAAU	1363	1826-1846	ATUCTUGAGUCCUUUUCCUUCAA	2844	1824-1846
AD-2017588.1	AAGGAAAAGGACUCAAGAAAU	1364	1827-1847	ATUUCUTGAGUCCUUUUCCUUCA	2845	1825-1847
AD-2017589.1	AGGAAAAGGACUCAAGAAAAU	1365	1828-1848	ATUUTCTUGAGTCCUUUUCCUUC	2846	1826-1848
AD-2017590.1	AAAAGACCAUAAAUAAGGGCU	1366	1853-1873	AGCCCUTAUUUAUGGUCUUUUAU	2847	1851-1873
AD-2017591.1	AUGUGAAAAGAAUGUAUUUCU	1367	1885-1905	AGAAAUACAUUCUUUUCACAUGG	2848	1883-1905
AD-2017592.1	UGUGAAAAGAAUGUAUUUCAU	1368	1886-1906	ATGAAATACAUTCUUUUCACAUG	2849	1884-1906
AD-2017593.1	GUGAAAAGAAUGUAUUUCACU	1369	1887-1907	AGUGAAAUACATUCUUUUCACAU	2850	1885-1907
AD-2017594.1	UGAAAAGAAUGUAUUUCACCU	1370	1888-1908	AGGUGAAAUACAUUCUUUUCACA	2851	1886-1908
AD-2017595.1	GAAAAGAAUGUAUUUCACCUU	1371	1889-1909	AAGGTGAAAUACAUUCUUUUCAC	2852	1887-1909
AD-2017596.1	AAAAGAAUGUAUUUCACCUGU	1372	1890-1910	ACAGGUGAAAUACAUUCUUUUCA	2853	1888-1910
AD-2017597.1	AAAGAAUGUAUUUCACCUGCU	1373	1891-1911	AGCAGGTGAAATACAUUCUUUUC	2854	1889-1911
AD-2017598.1	AAGAAUGUAUUUCACCUGCAU	1374	1892-1912	ATGCAGGUGAAAUACAUUCUUUU	2855	1890-1912
AD-2017599.1	AGAAUGUAUUUCACCUGCAAU	1375	1893-1913	ATUGCAGGUGAAAUACAUUCUUU	2856	1891-1913
AD-2017600.1	GAAUGUAUUUCACCUGCAAGU	1376	1894-1914	ACUUGCAGGUGAAAUACAUUCUU	2857	1892-1914
AD-2017601.1	AAUGUAUUUCACCUGCAAGUU	1377	1895-1915	AACUTGCAGGUGAAAUACAUUCU	2858	1893-1915
AD-2017602.1	AUGUAUUUCACCUGCAAGUUU	1378	1896-1916	AAACTUGCAGGTGAAAUACAUUC	2859	1894-1916
AD-2017603.1	UGUAUUUCACCUGCAAGUUAU	1379	1897-1917	ATAACUTGCAGGUGAAAUACAUU	2860	1895-1917
AD-2017604.1	GUAUUUCACCUGCAAGUUACU	1380	1898-1918	AGUAACTUGCAGGUGAAAUACAU	2861	1896-1918
AD-2017605.1	UAUUUCACCUGCAAGUUACAU	1381	1899-1919	ATGUAACUUGCAGGUGAAAUACA	2862	1897-1919
AD-2017606.1	AUUUCACCUGCAAGUUACAAU	1382	1900-1920	ATUGTAACUUGCAGGUGAAAUAC	2863	1898-1920

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017607.1	UUUCACCUGCAA GUUACAAAU	1383	1901-1921	ATUUGUAACUUG CAGGUGAAAUA	2864	1899-1921
AD-2017608.1	UUCACCUGCAAG UUACAAAAU	1384	1902-1922	ATUUTGTAACUTG CAGGUGAAAU	2865	1900-1922
AD-2017609.1	CCUGCAAGUUAC AAAAAAAUU	1385	1906-1926	AAUUTUTUUGUA ACUUGCAGGUG	2866	1904-1926
AD-2017610.1	CUGCAAGUUACA AAAAAAUAU	1386	1907-1927	ATAUTUTUUUGTA ACUUGCAGGU	2867	1905-1927
AD-2017611.1	UGCAAGUUACAA AAAAAUAGU	1387	1908-1928	ACUATUTUUUUG UAACUUGCAGG	2868	1906-1928
AD-2017612.1	GCAAGUUACAAA AAAAUAGUU	1388	1909-1929	AACUAUTUUUUT GUAACUUGCAG	2869	1907-1929
AD-2017613.1	AAGUUACAAAAA AAUAGUUUU	1389	1911-1931	AAAACUAUUUUT UUGUAACUUGC	2870	1909-1931
AD-2017614.1	UUACAAAAAAAU AGUUUGUGU	1390	1914-1934	ACACAAACUAUT UUUUUGUAACU	2871	1912-1934
AD-2017615.1	UACAAAAAAAUA GUUUGUGCU	1391	1915-1935	AGCACAAACUAT UUUUUUGUAAC	2872	1913-1935
AD-2017616.1	AAACCUUAGGAA AAAAAUGAU	1392	2000-2020	ATCATUTUUUUCC UAAGGUUUAA	2873	1998-2020
AD-2017617.1	AACCUUAGGAAA AAAAUGACU	1393	2001-2021	AGUCAUTUUUUTC CUAAGGUUUA	2874	1999-2021
AD-2017618.1	ACCUUAGGAAAA AAAUGACUU	1394	2002-2022	AAGUCATUUUUT UCCUAAGGUUU	2875	2000-2022
AD-2017619.1	CCUUAGGAAAAA AAUGACUUU	1395	2003-2023	AAAGTCAUUUUT UUCCUAAGGUU	2876	2001-2023
AD-2017620.1	CUUAGGAAAAAA AUGACUUGU	1396	2004-2024	ACAAGUCAUUUT UUUCCUAAGGU	2877	2002-2024
AD-2017621.1	UUAGGAAAAAA AUGACUUGGU	1397	2005-2025	ACCAAGTCAUUTU UUUCCUAAGG	2878	2003-2025
AD-2017622.1	UAGGAAAAAAA UGACUUGGUU	1398	2006-2026	AACCAAGUCAUT UUUUUCCUAAG	2879	2004-2026
AD-2017623.1	AGGAAAAAAAU GACUUGGUGU	1399	2007-2027	ACACCAAGUCATU UUUUUCCUAA	2880	2005-2027
AD-2017624.1	GGAAAAAAAUG ACUUGGUGUU	1400	2008-2028	AACACCAAGUCA UUUUUUUCCUA	2881	2006-2028
AD-2017625.1	GAAAAAAAUGAC UUGGUGUGU	1401	2009-2029	ACACACCAAGUC AUUUUUUUCCU	2882	2007-2029
AD-2017626.1	AAAAAAAUGACU UGGUGUGUU	1402	2010-2030	AACACACCAAGTC AUUUUUUUCC	2883	2008-2030
AD-2017627.1	AAAAAAUGACUU GGUGUGUUU	1403	2011-2031	AAACACACCAAG UCAUUUUUUUC	2884	2009-2031
AD-2017628.1	AAAAAUGACUUG GUGUGUUCU	1404	2012-2032	AGAACACACCAA GUCAUUUUUUU	2885	2010-2032
AD-2017629.1	AAAAUGACUUGG UGUGUUCUU	1405	2013-2033	AAGAACACACCA AGUCAUUUUUU	2886	2011-2033
AD-2017630.1	AAAUGACUUGGU GUGUUCUUU	1406	2014-2034	AAAGAACACACC AAGUCAUUUUU	2887	2012-2034

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017631.1	AAUGACUUGGUGUGUUCUUGU	1407	2015-2035	ACAAGAACACACCAAGUCAUUUU	2888	2013-2035
AD-2017632.1	AUGACUUGGUGUGUUCUUGUU	1408	2016-2036	AACAAGAACACACCAAGUCAUUU	2889	2014-2036
AD-2017633.1	UGACUUGGUGUGUUCUUGUGU	1409	2017-2037	ACACAAGAACACACCAAGUCAUU	2890	2015-2037
AD-2017634.1	GACUUGGUGUGUUCUUGUGUU	1410	2018-2038	AACACAAGAACACACCAAGUCAU	2891	2016-2038
AD-2017635.1	ACUUGGUGUGUUCUUGUGUGU	1411	2019-2039	ACACACAAGAACACACCAAGUCA	2892	2017-2039
AD-2017636.1	CUUGGUGUGUUCUUGUGUGAU	1412	2020-2040	ATCACACAAGAACACACCAAGUC	2893	2018-2040
AD-2017637.1	UUGGUGUGUUCUUGUGUGAUU	1413	2021-2041	AAUCACACAAGAACACACCAAGU	2894	2019-2041
AD-2017638.1	UGGUGUGUUCUUGUGUGAUUU	1414	2022-2042	AAAUCACACAAGAACACACCAAG	2895	2020-2042
AD-2017639.1	GGUGUGUUCUUGUGUGAUUUU	1415	2023-2043	AAAATCACACAAGAACACACCAA	2896	2021-2043
AD-2017640.1	GUGUGUUCUUGUGUGAUUUUU	1416	2024-2044	AAAAAUCACACAAGAACACACCA	2897	2022-2044
AD-2017641.1	UGUGUUCUUGUGUGAUUUUUU	1417	2025-2045	AAAAAATCACACAAGAACACACC	2898	2023-2045
AD-2017642.1	GUGUUCUUGUGUGAUUUUUAU	1418	2026-2046	ATAAAAAUCACACAAGAACACAC	2899	2024-2046
AD-2017643.1	UGUUCUUGUGUGAUUUUUACU	1419	2027-2047	AGUAAAAAUCACACAAGAACACA	2900	2025-2047
AD-2017644.1	GUUCUUGUGUGAUUUUUACAU	1420	2028-2048	ATGUAAAAAUCACACAAGAACAC	2901	2026-2048
AD-2017645.1	UUCUUGUGUGAUUUUUACAUU	1421	2029-2049	AAUGTAAAAAUCACACAAGAACA	2902	2027-2049
AD-2017646.1	UCUUGUGUGAUUUUUACAUUU	1422	2030-2050	AAAUGUAAAAATCACACAAGAAC	2903	2028-2050
AD-2017647.1	CUUGUGUGAUUUUUACAUUGU	1423	2031-2051	ACAATGTAAAAAUCACACAAGAA	2904	2029-2051
AD-2017648.1	UUGUGUGAUUUUUACAUUGCU	1424	2032-2052	AGCAAUGUAAAAAUCACACAAGA	2905	2030-2052
AD-2017649.1	UGUGUGAUUUUUACAUUGCUU	1425	2033-2053	AAGCAATGUAAAAAUCACACAAG	2906	2031-2053
AD-2017650.1	GUGUGAUUUUUACAUUGCUAU	1426	2034-2054	ATAGCAAUGUAAAAAUCACACAA	2907	2032-2054
AD-2017651.1	UGUGAUUUUUACAUUGCUAUU	1427	2035-2055	AAUAGCAAUGUAAAAAUCACACA	2908	2033-2055
AD-2017652.1	GUGAUUUUUACAUUGCUAUAU	1428	2036-2056	ATAUAGCAAUGTAAAAAUCACAC	2909	2034-2056
AD-2017653.1	UGCAUAUUUAAAACAUGUCUU	1429	2072-2092	AAGACATGUUUTAAAUAUGCAUA	2910	2070-2092
AD-2017654.1	GCAUAUUUAAAACAUGUCUCU	1430	2073-2093	AGAGACAUGUUTUAAAUAUGCAU	2911	2071-2093

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017655.1	CAUAUUUAAAAC AUGUCUCCU	1431	2074-2094	AGGAGACAUGUT UUAAAUAUGCA	2912	2072-2094
AD-2017656.1	AUAUUUAAAACA UGUCUCCCU	1432	2075-2095	AGGGAGACAUGT UUUAAAUAUGC	2913	2073-2095
AD-2017657.1	UAUUUAAAACAU GUCUCCCUU	1433	2076-2096	AAGGGAGACAUG UUUUAAAUAUG	2914	2074-2096
AD-2017658.1	AUUUAAAACAUG UCUCCCUUU	1434	2077-2097	AAAGGGAGACAT GUUUUAAAUAU	2915	2075-2097
AD-2017659.1	UUUAAAACAUGU CUCCCUUAU	1435	2078-2098	ATAAGGGAGACA UGUUUUAAAUA	2916	2076-2098
AD-2017660.1	UUAAAACAUGUC UCCCUUAUU	1436	2079-2099	AAUAAGGGAGAC AUGUUUUAAAU	2917	2077-2099
AD-2017661.1	UAAAACAUGUCU CCCUUAUUU	1437	2080-2100	AAAUAAGGGAGA CAUGUUUUAAA	2918	2078-2100
AD-2017662.1	AAAACAUGUCUC CCUUAUUUU	1438	2081-2101	AAAATAAGGGAG ACAUGUUUUAA	2919	2079-2101
AD-2017663.1	AAACAUGUCUCC CUUAUUUAU	1439	2082-2102	ATAAAUAAGGGA GACAUGUUUUA	2920	2080-2102
AD-2017664.1	AACAUGUCUCCC UUAUUUACU	1440	2083-2103	AGUAAATAAGGG AGACAUGUUUU	2921	2081-2103
AD-2017665.1	ACAUGUCUCCCU UAUUUACCU	1441	2084-2104	AGGUAAAUAAGG GAGACAUGUUU	2922	2082-2104
AD-2017666.1	CAUGUCUCCCUU AUUUACCAU	1442	2085-2105	ATGGTAAAUAAG GGAGACAUGUU	2923	2083-2105
AD-2017667.1	AUGUCUCCCUUA UUUACCAUU	1443	2086-2106	AAUGGUAAAUAA GGGAGACAUGU	2924	2084-2106
AD-2017669.1	GUCUCCCUUAUU UACCAUAUU	1444	2088-2108	AAUATGGUAAAT AAGGGAGACAU	2925	2086-2108
AD-2017670.1	AAUUCUGAAACA CAAAAUAUU	1445	2119-2139	AAUATUTUGUGTU UCAGAAUUCU	2926	2117-2139
AD-2017671.1	AUUCUGAAACAC AAAAUAUGU	1446	2120-2140	ACAUAUTUUGUG UUUCAGAAUUC	2927	2118-2140
AD-2017672.1	CAAAAUAUGAAA UAAAUUGGU	1447	2131-2151	ACCAAUTUAUUTC AUAUUUUGUG	2928	2129-2151
AD-2017673.1	AAAUAUGAAAU AAAUUGGGAU	1448	2133-2153	ATCCCAAUUUATU UCAUAUUUUG	2929	2131-2153
AD-2017674.1	AUAUGAAAUAA AUUGGGAGUU	1449	2135-2155	AACUCCCAAUUTA UUUCAUAUUU	2930	2133-2155
AD-2017675.1	UAUGAAAUAAA UUGGGAGUCU	1450	2136-2156	AGACTCCCAAUTU AUUUCAUAUU	2931	2134-2156
AD-2017676.1	AUGAAAUAAAU UGGGAGUCAU	1451	2137-2157	ATGACUCCCAATU UAUUUCAUAU	2932	2135-2157
AD-2017677.1	UGAAAUAAAUU GGGAGUCAGU	1452	2138-2158	ACUGACTCCCAAU UUAUUUCAUA	2933	2136-2158
AD-2017678.1	GAAAUAAAUUG GGAGUCAGGU	1453	2139-2159	ACCUGACUCCCAA UUUAUUUCAU	2934	2137-2159
AD-2017679.1	AAAUAAAUUGG GAGUCAGGAU	1454	2140-2160	ATCCTGACUCCCA AUUUAUUUCA	2935	2138-2160

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017680.1	AAUAAAUUGGGAGUCAGGAAU	1455	2141-2161	ATUCCUGACUCCCAAUUUAUUUC	2936	2139-2161
AD-2017681.1	AUAAAUUGGGAGUCAGGAAUU	1456	2142-2162	AAUUCCUGACUCCCAAUUUAUUU	2937	2140-2162
AD-2017682.1	UAAAUUGGGAGUCAGGAAUAU	1457	2143-2163	ATAUTCCUGACTCCCAAUUUAUU	2938	2141-2163
AD-2017683.1	AAAUUGGGAGUCAGGAAUAAU	1458	2144-2164	ATUATUCCUGACUCCCAAUUUAU	2939	2142-2164
AD-2017684.1	AAUUGGGAGUCAGGAAUAAUU	1459	2145-2165	AAUUAUTCCUGACUCCCAAUUUA	2940	2143-2165
AD-2017685.1	AUUGGGAGUCAGGAAUAAUUU	1460	2146-2166	AAAUTATUCCUGACUCCCAAUUU	2941	2144-2166
AD-2017686.1	UUGGGAGUCAGGAAUAAUUAU	1461	2147-2167	ATAATUAUUCCTGACUCCCAAUU	2942	2145-2167
AD-2017687.1	UGGGAGUCAGGAAUAAUUAUU	1462	2148-2168	AAUAAUTAUUCCUGACUCCCAAU	2943	2146-2168
AD-2017688.1	GGGAGUCAGGAAUAAUUAUUU	1463	2149-2169	AAAUAATUAUUCCUGACUCCCAA	2944	2147-2169
AD-2017689.1	GGAGUCAGGAAUAAUUAUUUU	1464	2150-2170	AAAATAAUUAUTCCUGACUCCCA	2945	2148-2170
AD-2017690.1	GAGUCAGGAAUAAUUAUUUGU	1465	2151-2171	ACAAAUAAUUATUCCUGACUCCC	2946	2149-2171
AD-2017691.1	AGUCAGGAAUAAUUAUUUGUU	1466	2152-2172	AACAAATAAUUAUUCCUGACUCC	2947	2150-2172
AD-2017692.1	GUCAGGAAUAAUUAUUUGUGU	1467	2153-2173	ACACAAAUAAUTAUUCCUGACUC	2948	2151-2173
AD-2017693.1	GCACUAAAUUUCAAUUAUACU	1468	2172-2192	AGUATAAUUGAAAUUUAGUGCAC	2949	2170-2192
AD-2017694.1	CAAUUAAAAGAAACUAUCCAU	1469	2228-2248	ATGGAUAGUUUCUUUUAAUUGAU	2950	2226-2248
AD-2017695.1	AAUUAAAAGAAACUAUCCACU	1470	2229-2249	AGUGGATAGUUTCUUUUAAUUGA	2951	2227-2249
AD-2017696.1	AUUAAAAGAAACUAUCCACAU	1471	2230-2250	ATGUGGAUAGUTUCUUUUAAUUG	2952	2228-2250
AD-2017697.1	UUAAAAGAAACUAUCCACAAU	1472	2231-2251	ATUGTGGAUAGTUUCUUUUAAUU	2953	2229-2251
AD-2017698.1	UAAAAGAAACUAUCCACAACU	1473	2232-2252	AGUUGUGGAUAGUUUCUUUUAAU	2954	2230-2252
AD-2017699.1	AAAAGAAACUAUCCACAACCU	1474	2233-2253	AGGUTGTGGAUAGUUUCUUUUAA	2955	2231-2253
AD-2017700.1	AAAGAAACUAUCCACAACCUU	1475	2234-2254	AAGGTUGUGGATAGUUUCUUUUA	2956	2232-2254
AD-2017701.1	AAGAAACUAUCCACAACCUGU	1476	2235-2255	ACAGGUTGUGGAUAGUUUCUUUU	2957	2233-2255
AD-2017702.1	AGAAACUAUCCACAACCUGUU	1477	2236-2256	AACAGGTUGUGGAUAGUUUCUUU	2958	2234-2256
AD-2017703.1	GAAACUAUCCACAACCUGUUU	1478	2237-2257	AAACAGGUUGUGGAUAGUUUCUU	2959	2235-2257

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017704.1	AAACUAUCCACA ACCUGUUAU	1479	2238-2258	ATAACAGGUUGT GGAUAGUUUCU	2960	2236-2258
AD-2017705.1	AACUAUCCACAA CCUGUUAAU	1480	2239-2259	ATUAACAGGUUG UGGAUAGUUUC	2961	2237-2259
AD-2017706.1	ACUAUCCACAAC CUGUUAAUU	1481	2240-2260	AAUUAACAGGUT GUGGAUAGUUU	2962	2238-2260
AD-2017707.1	CUAUCCACAACC UGUUAAUGU	1482	2241-2261	ACAUTAACAGGTU GUGGAUAGUU	2963	2239-2261
AD-2017708.1	UAUCCACAACCU GUUAAUGAU	1483	2242-2262	ATCATUAACAGGU UGUGGAUAGU	2964	2240-2262
AD-2017709.1	AUCCACAACCUG UUAAUGAAU	1484	2243-2263	ATUCAUTAACAGG UUGUGGAUAG	2965	2241-2263
AD-2017710.1	UCCACAACCUGU UAAUGAAAU	1485	2244-2264	ATUUCATUAACAG GUUGUGGAUA	2966	2242-2264
AD-2017711.1	CCACAACCUGUU AAUGAAACU	1486	2245-2265	AGUUTCAUUAAC AGGUUGUGGAU	2967	2243-2265
AD-2017712.1	CACAACCUGUUA AUGAAACUU	1487	2246-2266	AAGUTUCAUUAA CAGGUUGUGGA	2968	2244-2266
AD-2017713.1	ACAACCUGUUAA UGAAACUAU	1488	2247-2267	ATAGTUTCAUUAA CAGGUUGUGG	2969	2245-2267
AD-2017714.1	CAACCUGUUAAU GAAACUAAU	1489	2248-2268	ATUAGUTUCAUTA ACAGGUUGUG	2970	2246-2268
AD-2017715.1	AACCUGUUAAUG AAACUAAAU	1490	2249-2269	ATUUAGTUUCATU AACAGGUUGU	2971	2247-2269
AD-2017716.1	ACCUGUUAAUGA AACUAAAAU	1491	2250-2270	ATUUTAGUUUCA UUAACAGGUUG	2972	2248-2270
AD-2017717.1	CCUGUUAAUGAA ACUAAAAAU	1492	2251-2271	ATUUTUAGUUUC AUUAACAGGUU	2973	2249-2271
AD-2017718.1	CUGUUAAUGAAA CUAAAAACU	1493	2252-2272	AGUUTUTAGUUTC AUUAACAGGU	2974	2250-2272
AD-2017719.1	UGUUAAUGAAAC UAAAAACUU	1494	2253-2273	AAGUTUTUAGUTU CAUUAACAGG	2975	2251-2273
AD-2017722.1	GGUUUAUGAUCA UCUUAAAAU	1495	2295-2315	ATUUTAAGAUGA UCAUAAACCCG	2976	2293-2315
AD-2017723.1	GUUUAUGAUCAU CUUAAAAUU	1496	2296-2316	AAUUTUAAGAUG AUCAUAAACCC	2977	2294-2316
AD-2017725.1	AAUCAUAUUUUG AGAUAGUAU	1497	2318-2338	ATACTATCUCAAA AUAUGAUUUC	2978	2316-2338
AD-2017726.1	AUCAUAUUUUGA GAUAGUAGU	1498	2319-2339	ACUACUAUCUCA AAAUAUGAUUU	2979	2317-2339
AD-2017727.1	UUUAAACCAUUU UGAAAUAUU	1499	2340-2360	AAUATUTCAAAA UGGUUUAAAGC	2980	2338-2360
AD-2017728.1	AAAUAUGUUGA UUUUUUCCAU	1500	2354-2374	ATGGAAAAAAUC AACAUAUUUCA	2981	2352-2374
AD-2017730.1	AUAUGUUGAUU UUUUCCAGGU	1501	2356-2376	ACCUGGAAAAAA UCAACAUAUUU	2982	2354-2376
AD-2017731.1	UAUGUUGAUUU UUUCCAGGUU	1502	2357-2377	AACCTGGAAAAA AUCAACAUAUU	2983	2355-2377

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3	Antisense Sequence 5' to 3'	SEQ ID NO:	Range in NM_004490.3
AD-2017732.1	AUGUUGAUUUUUUCCAGGUAU	1503	2358-2378	ATACCUGGAAAAAAUCAACAUAU	2984	2356-2378
AD-2017733.1	UGUUGAUUUUUUCCAGGUAAU	1504	2359-2379	ATUACCTGGAAAAAAUCAACAUA	2985	2357-2379
AD-2017734.1	GUUGAUUUUUUCCAGGUAAUU	1505	2360-2380	AAUUACCUGGAAAAAAUCAACAU	2986	2358-2380

Table 3. Human Modified Sense and Antisense Strand Sequences of GRB14 dsRNA Agents

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1947923	gcgacaauGfAfCfcacuucccuu	2987	PadAggdGadAguggdTcAfuugucgccg	4468	CGGCGACAAUGACCACUUCCCUG	5949
AD-1947924	gcgacaAfuGfAfCfcacuucccuu	2988	PaAfggdGa(Agn)guggucAfuUfgucgccg	4469	CGGCGACAAUGACCACUUCCCUG	5950
AD-1947925	gacaaugaCfCfAfcuucccugcu	2989	PadGcadGgdGaagudGgUfcauugucgc	4470	GCGACAAUGACCACUUCCCUGCA	5951
AD-1947926	acaaugacCfAfCfuucccugcau	2990	PadTgcdAgdGgaagdTgGfucauugucg	4471	CGACAAUGACCACUUCCCUGCAA	5952
AD-1947927	caaugaccAfCfUfuccugcaau	2991	PadTugdCadGggaadGuGfgucauuguc	4472	GACAAUGACCACUUCCCUGCAAG	5953
AD-1947928	aaugaccaCfUfUfccugcaagu	2992	PadCuudGcdAgggadAgUfggucauugu	4473	ACAAUGACCACUUCCCUGCAAGA	5954
AD-1947929	aaugacCfaCfUfUfccugcaagu	2993	PaCfuudGc(Agn)gggaagUfgGfucauugu	4474	ACAAUGACCACUUCCCUGCAAGA	5955
AD-1947930	ugaccacuUfCfCfcugcaagauu	2994	PadAucdTudGcaggdGaAfguggucauu	4475	AAUGACCACUUCCCUGCAAGAUG	5956
AD-1947931	gaccacuuCfCfCfugcaagaugu	2995	PadCaudCudTgcagdGgAfaguggucau	4476	AUGACCACUUCCCUGCAAGAUGG	5957
AD-1947932	accacuucCfCfUfgcaagauggu	2996	PadCcadTcdTugcadGgGfaagugguca	4477	UGACCACUUCCCUGCAAGAUGGG	5958
AD-1947933	accacuUfcCfCfUfgcaagauggu	2997	PaCfcadTc(Tgn)ugcaggGfaAfgugguca	4478	UGACCACUUCCCUGCAAGAUGGG	5959
AD-1947934	uucccugcAfAfGfaugggcagau	2998	PadTcudGcdCcaucdTuGfcagggaagu	4479	ACUUCCCUGCAAGAUGGGCAGAG	5960
AD-1947935	ucccugcaAfGfAfugggcagagu	2999	PadCucdTgdCccaudCuUfgcagggaag	4480	CUUCCCUGCAAGAUGGGCAGAGC	5961
AD-1947936	cccugcaaGfAfUfggcagagcu	3000	PadGcudCudGcccadTcUfugcagggaa	4481	UUCCCUGCAAGAUGGGCAGAGCG	5962
AD-1947937	gcugcagaCfAfGfgagaaaaaau	3001	PadTuudTudTcuccdTgUfcugcagcac	4482	GUGCUGCAGACAGGAGAAAAAAG	5963
AD-1947938	gcugcaGfaCfAfGfgagaaaaaau	3002	PaUfuudTu(Tgn)cuccugUfcUfgcagcac	4483	GUGCUGCAGACAGGAGAAAAAAG	5964
AD-1947939	cugcagacAfGfGfagaaaaaagu	3003	PadCuudTudTucucdCuGfucugcagca	4484	UGCUGCAGACAGGAGAAAAAAGA	5965
AD-1947940	ugcagacaGfGfAfgaaaaaagau	3004	PadTcudTudTuucudCcUfgucugcagc	4485	GCUGCAGACAGGAGAAAAAAGAA	5966

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1947941	ugcagaCfaGfGfAfgaaaaaagau	3005	PaUfcudTu(Tgn)uucuccUfgUfcugcagc	4486	GCUGCAGACAGGAGAAAAAAGAA	5967
AD-1947942	gcagacagGfAfGfaaaaaagaau	3006	PadTucdTudTuuucdTcCfugucugcag	4487	CUGCAGACAGGAGAAAAAAGAAA	5968
AD-1947943	gcagacAfgGfAfGfaaaaaagaau	3007	PaUfucdTu(Tgn)uuucucCfuGfucugcag	4488	CUGCAGACAGGAGAAAAAAGAAA	5969
AD-1947944	cagacaggAfGfAfaaaaagaaau	3008	PadTuudCudTuuuudCuCfcugucugca	4489	UGCAGACAGGAGAAAAAGAAAG	5970
AD-1947945	cagacaGfgAfGfAfaaaaagaaau	3009	PaUfuudCu(Tgn)uuuucuCfcUfgucugca	4490	UGCAGACAGGAGAAAAAGAAAG	5971
AD-1947946	gacaggagAfAfAfaaagaaagau	3010	PadTcudTudCuuuudTuCfuccugucug	4491	CAGACAGGAGAAAAAAGAAAGAU	5972
AD-1947947	acaggagaAfAfAfaagaaagauu	3011	PadAucdTudTcuuudTuUfcuccugucu	4492	AGACAGGAGAAAAAAGAAAGAUC	5973
AD-1947948	acaggaGfaAfAfAfaagaaagauu	3012	PaAfucdTu(Tgn)cuuuuuUfcUfccugucu	4493	AGACAGGAGAAAAAAGAAAGAUC	5974
AD-1947949	caggagaaAfAfAfagaaagaucu	3013	PadGaudCudTucuudTuUfucuccuguc	4494	GACAGGAGAAAAAAGAAAGAUCU	5975
AD-1947950	caggagAfaAfAfAfagaaagaucu	3014	PaGfaudCu(Tgn)ucuuuuUfuCfuccuguc	4495	GACAGGAGAAAAAAGAAAGAUCU	5976
AD-1947951	aggagaaaAfAfAfgaaagaucuu	3015	PadAgadTcdTuucudTuUfuucuccugu	4496	ACAGGAGAAAAAAGAAAGAUCUU	5977
AD-1947952	aggagaAfaAfAfAfgaaagaucuu	3016	PaAfgadTc(Tgn)uucuuuUfuUfcuccugu	4497	ACAGGAGAAAAAAGAAAGAUCUU	5978
AD-1947953	ggagaaaaAfAfGfaaagaucuuu	3017	PadAagdAudCuuucdTuUfuuucuccug	4498	CAGGAGAAAAAAGAAAGAUCUUG	5979
AD-1947954	gagaaaaaAfGfAfaagaucuugu	3018	PadCaadGadTcuuudCuUfuuuucuccu	4499	AGGAGAAAAAAGAAAGAUCUUGA	5980
AD-1947955	agaaaaaaGfAfAfagaucuugau	3019	PadTcadAgdAucuudTcUfuuuuucucc	4500	GGAGAAAAAAGAAAGAUCUUGAU	5981
AD-1947956	agaaaaAfaGfAfAfagaucuugau	3020	PaUfcadAg(Agn)ucuuucUfuUfuuucucc	4501	GGAGAAAAAAGAAAGAUCUUGAU	5982
AD-1947957	gaaaaaagAfAfAfgaucuugauu	3021	PadAucdAadGaucudTuCfuuuuuucuc	4502	GAGAAAAAAGAAAGAUCUUGAUG	5983
AD-1947958	aaaaaagaAfAfGfaucuugaugu	3022	PadCaudCadAgaucdTuUfcuuuuuucu	4503	AGAAAAAAGAAAGAUCUUGAUGU	5984
AD-1947959	aaaaagaaAfGfAfucuugauguu	3023	PadAcadTcdAagaudCuUfucuuuuuuc	4504	GAAAAAAGAAAGAUCUUGAUGUU	5985
AD-1947960	aaaagaaaGfAfUfcugauguuu	3024	PadAacdAudCaagadTcUfuucuuuuuu	4505	AAAAAAGAAAGAUCUUGAUGUUC	5986
AD-1947961	aaagaaagAfUfCfuugauguucu	3025	PadGaadCadTcaagdAuCfuuucuuuuu	4506	AAAAAGAAAGAUCUUGAUGUUCC	5987
AD-1947962	aaagaaAfgAfUfCfuugauguucu	3026	PaGfaadCa(Tgn)caagauCfuUfucuuuuu	4507	AAAAAGAAAGAUCUUGAUGUUCC	5988
AD-1947963	aagaaagaUfCfUfugauguuccu	3027	PadGgadAcdAucaadGaUfcuuucuuuu	4508	AAAAGAAAGAUCUUGAUGUUCCG	5989
AD-1947964	aagaaaGfaUfCfUfugauguuccu	3028	PaGfgadAc(Agn)ucaagaUfcUfuucuuuu	4509	AAAAGAAAGAUCUUGAUGUUCCG	5990

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1947965	agaaagauCfUfUfgauguuccgu	3029	PadCggdAadCaucadAgAfucuuucuuu	4510	AAAGAAAGAUCUUGAUGUUCCGG	5991
AD-1947966	aaagaucuUfGfAfuguuccggau	3030	PadTccdGgdAacaudCaAfgaucuuucu	4511	AGAAAGAUCUUGAUGUUCCGGAA	5992
AD-1947967	aagaucuuGfAfUfguuccggaau	3031	PadTucdCgdGaacadTcAfagaucuuuc	4512	GAAAGAUCUUGAUGUUCCGGAAA	5993
AD-1947968	agaucuugAfUfGfuuccggaaau	3032	PadTuudCcdGgaacdAuCfaagaucuuu	4513	AAAGAUCUUGAUGUUCCGGAAAU	5994
AD-1947969	gaucuugaUfGfUfuccggaaauu	3033	PadAuudTcdCggaadCaUfcaagaucuu	4514	AAGAUCUUGAUGUUCCGGAAAUG	5995
AD-1947970	aucuugauGfUfUfccggaaaugu	3034	PadCaudTudCcggadAcAfucaagaucu	4515	AGAUCUUGAUGUUCCGGAAAUGC	5996
AD-1947971	ucuugaugUfUfCfcggaaaugcu	3035	PadGcadTudTccggdAaCfaucaagauc	4516	GAUCUUGAUGUUCCGGAAAUGCC	5997
AD-1947972	cuugauguUfCfCfggaaaugccu	3036	PadGgcdAudTuccgdGaAfcaucaagau	4517	AUCUUGAUGUUCCGGAAAUGCCA	5998
AD-1947973	cuugauGfuUfCfCfggaaaugccu	3037	PaGfgcdAu(Tgn)uccggaAfcAfucaagau	4518	AUCUUGAUGUUCCGGAAAUGCCA	5999
AD-1947974	uugauguuCfCfGfgaaaugccau	3038	PadTggdCadTuuccdGgAfacaucaaga	4519	UCUUGAUGUUCCGGAAAUGCCAU	6000
AD-1947975	uugaugUfuCfCfGfgaaaugccau	3039	PaUfggdCa(Tgn)uuccggAfaCfaucaaga	4520	UCUUGAUGUUCCGGAAAUGCCAU	6001
AD-1947976	ugauguucCfGfGfaaaugccauu	3040	PadAugdGcdAuuucdCgGfaacaucaag	4521	CUUGAUGUUCCGGAAAUGCCAUC	6002
AD-1947977	ugauguUfcCfGfGfaaaugccauu	3041	PaAfugdGc(Agn)uuuccgGfaAfcaucaag	4522	CUUGAUGUUCCGGAAAUGCCAUC	6003
AD-1947978	gauguuccGfGfAfaaugccaucu	3042	PadGaudGgdCauuudCcGfgaacaucaa	4523	UUGAUGUUCCGGAAAUGCCAUCU	6004
AD-1947979	auguuccgGfAfAfaugccaucuu	3043	PadAgadTgdGcauudTcCfggaacauca	4524	UGAUGUUCCGGAAAUGCCAUCUA	6005
AD-1947980	uguuccggAfAfAfugccaucuau	3044	PadTagdAudGgcaudTuCfcggaacauc	4525	GAUGUUCCGGAAAUGCCAUCUAU	6006
AD-1947981	guuccggaAfAfUfgccaucuauu	3045	PadAuadGadTggcadTuUfccggaacau	4526	AUGUUCCGGAAAUGCCAUCUAUU	6007
AD-1947982	guuccgGfaAfAfUfgccaucuauu	3046	PaAfuadGa(Tgn)ggcauuUfcCfggaacau	4527	AUGUUCCGGAAAUGCCAUCUAUU	6008
AD-1947983	uuccggaaAfUfGfccaucuauuu	3047	PadAaudAgdAuggcdAuUfuccggaaca	4528	UGUUCCGGAAAUGCCAUCUAUUC	6009
AD-1947984	uuccggAfaAfUfGfccaucuauuu	3048	PaAfaudAg(Agn)uggcauUfuCfcggaaca	4529	UGUUCCGGAAAUGCCAUCUAUUC	6010
AD-1947985	uccggaaaUfGfCfcaucuauucu	3049	PadGaadTadGauggdCaUfuuccggaac	4530	GUUCCGGAAAUGCCAUCUAUUCC	6011
AD-1947986	ccggaaauGfCfCfaucuauuccu	3050	PadGgadAudAgaugdGcAfuuuccggaa	4531	UUCCGGAAAUGCCAUCUAUUCCA	6012
AD-1947987	cggaaaugCfCfAfucuauuccau	3051	PadTggdAadTagaudGgCfauuuccgga	4532	UCCGGAAAUGCCAUCUAUUCCAA	6013
AD-1947988	cggaaaUfgCfCfAfucuauuccau	3052	PaUfggdAa(Tgn)agauggCfaUfuuccgga	4533	UCCGGAAAUGCCAUCUAUUCCAA	6014

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1947989	ggaaaugcCfAfUfcuauuccaau	3053	PadTugdGadAuagadTgGfcauuuccgg	4534	CCGGAAAUGCCAUCUAUUCCAAA	6015
AD-1947990	ggaaauGfcCfAfUfcuauuccaau	3054	PaUfugdGa(Agn)uagaugGfcAfuuuccgg	4535	CCGGAAAUGCCAUCUAUUCCAAA	6016
AD-1947991	gaaaugccAfUfCfuauuccaaau	3055	PadTuudGgdAauagdAuGfgcauuuccg	4536	CGGAAAUGCCAUCUAUUCCAAAC	6017
AD-1947992	gaaaugCfcAfUfCfuauuccaaau	3056	PaUfuudGg(Agn)auagauGfgCfauuuccg	4537	CGGAAAUGCCAUCUAUUCCAAAC	6018
AD-1947993	aaaugccaUfCfUfauuccaaacu	3057	PadGuudTgdGaauadGaUfggcauuucc	4538	GGAAAUGCCAUCUAUUCCAAACC	6019
AD-1947994	aaugccauCfUfAfuuccaaaccu	3058	PadGgudTudGgaaudAgAfuggcauuuc	4539	GAAAUGCCAUCUAUUCCAAACCC	6020
AD-1947995	augccaucUfAfUfuccaaacccu	3059	PadGggdTudTggaadTaGfauggcauuu	4540	AAAUGCCAUCUAUUCCAAACCCU	6021
AD-1947996	augccaUfcUfAfUfuccaaacccu	3060	PaGfggdTu(Tgn)ggaauaGfaUfggcauuu	4541	AAAUGCCAUCUAUUCCAAACCCU	6022
AD-1947997	ugccaucuAfUfUfccaaacccuu	3061	PadAggdGudTuggadAuAfgauggcauu	4542	AAUGCCAUCUAUUCCAAACCCUU	6023
AD-1947998	ugccauCfuAfUfUfccaaacccuu	3062	PaAfggdGu(Tgn)uggaauAfgAfuggcauu	4543	AAUGCCAUCUAUUCCAAACCCUU	6024
AD-1947999	gccaucuaUfUfCfcaaacccuuu	3063	PadAagdGgdTuuggdAaUfagauggcau	4544	AUGCCAUCUAUUCCAAACCCUUU	6025
AD-1948000	gccaucUfaUfUfCfcaaacccuuu	3064	PaAfagdGg(Tgn)uuggaaUfaGfauggcau	4545	AUGCCAUCUAUUCCAAACCCUUU	6026
AD-1948001	ccaucuauUfCfCfaaacccuuuu	3065	PadAaadGgdGuuugdGaAfuagauggca	4546	UGCCAUCUAUUCCAAACCCUUUU	6027
AD-1948002	caucuauuCfCfAfaacccuuuuu	3066	PadAaadAgdGguuudGgAfauagauggc	4547	GCCAUCUAUUCCAAACCCUUUUC	6028
AD-1948003	aucuauucCfAfAfaccuuuucu	3067	PadGaadAadGgguudTgGfaauagaugg	4548	CCAUCUAUUCCAAACCCUUUUCC	6029
AD-1948004	ucuauuccAfAfAfccuuuuccu	3068	PadGgadAadAgggudTuGfgaauagaug	4549	CAUCUAUUCCAAACCCUUUUCCU	6030
AD-1948005	cuauuccaAfAfCfccuuuuccuu	3069	PadAggdAadAagggdTuUfggaauagau	4550	AUCUAUUCCAAACCCUUUUCCUG	6031
AD-1948006	uauuccaaAfCfCfcuuuuccugu	3070	PadCagdGadAaaggdGuUfuggaauaga	4551	UCUAUUCCAAACCCUUUUCCUGA	6032
AD-1948007	auuccaaaCfCfCfuuuuccugau	3071	PadTcadGgdAaaagdGgUfuuggaauag	4552	CUAUUCCAAACCCUUUUCCUGAG	6033
AD-1948008	auuccaAfaCfCfCfuuuuccugau	3072	PaUfcadGg(Agn)aaagggUfuUfggaauag	4553	CUAUUCCAAACCCUUUUCCUGAG	6034
AD-1948009	uuccaaacCfCfUfuuuccugagu	3073	PadCucdAgdGaaaadGgGfuuuggaaua	4554	UAUUCCAAACCCUUUUCCUGAGC	6035
AD-1948010	uccaaaccCfUfUfuuccugagcu	3074	PadGcudCadGgaaadAgGfguuuggaau	4555	AUUCCAAACCCUUUUCCUGAGCU	6036
AD-1948011	ccaaacccUfUfUfuccugagcuu	3075	PadAgcdTcdAggaadAaGfgguuuggaa	4556	UUCCAAACCCUUUUCCUGAGCUA	6037
AD-1948012	ccaaacCfcUfUfUfuccugagcuu	3076	PaAfgcdTc(Agn)ggaaaaGfgGfuuuggaa	4557	UUCCAAACCCUUUUCCUGAGCUA	6038

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948013	caaacccuUfUfUfccugagcuau	3077	PadTagdCudCaggadAaAfggguuugga	4558	UCCAAACCCUUUUCCUGAGCUAU	6039
AD-1948014	aaacccuuUfUfCfcugagcuauu	3078	PadAuadGcdTcaggdAaAfaggguuugg	4559	CCAAACCCUUUUCCUGAGCUAUG	6040
AD-1948015	aaacccUfuUfUfCfcugagcuauu	3079	PaAfuadGc(Tgn)caggaaAfaGfgguuugg	4560	CCAAACCCUUUUCCUGAGCUAUG	6041
AD-1948016	aacccuuuUfCfCfugagcuaugu	3080	PadCaudAgdCucagdGaAfaaggguuug	4561	CAAACCCUUUUCCUGAGCUAUGC	6042
AD-1948017	cccuuuucCfUfGfagcuaugcuu	3081	PadAgcdAudAgcucdAgGfaaaaggguu	4562	AACCCUUUUCCUGAGCUAUGCUG	6043
AD-1948018	ccuuuuccUfGfAfgcuaugcugu	3082	PadCagdCadTagcudCaGfgaaaagggu	4563	ACCCUUUUCCUGAGCUAUGCUGU	6044
AD-1948019	cuuuuccuGfAfGfcuaugcuguu	3083	PadAcadGcdAuagcdTcAfggaaaaggg	4564	CCCUUUUCCUGAGCUAUGCUGUU	6045
AD-1948020	cuuuucCfuGfAfGfcuaugcuguu	3084	PaAfcadGc(Agn)uagcucAfgGfaaaaggg	4565	CCCUUUUCCUGAGCUAUGCUGUU	6046
AD-1948021	uuuuccugAfGfCfuaugcuguuu	3085	PadAacdAgdCauagdCuCfaggaaaagg	4566	CCUUUUCCUGAGCUAUGCUGUUC	6047
AD-1948022	uuuccugaGfCfUfaugcuguucu	3086	PadGaadCadGcauadGcUfcaggaaaag	4567	CUUUUCCUGAGCUAUGCUGUUCU	6048
AD-1948023	uuccugagCfUfAfugcuguucuu	3087	PadAgadAcdAgcaudAgCfucaggaaaa	4568	UUUUCCUGAGCUAUGCUGUUCUC	6049
AD-1948024	uuccugAfgCfUfAfugcuguucuu	3088	PaAfgadAc(Agn)gcauagCfuCfaggaaaa	4569	UUUUCCUGAGCUAUGCUGUUCUC	6050
AD-1948025	ccugagcuAfUfGfcuguucuccu	3089	PadGgadGadAcagcdAuAfgcucaggaa	4570	UUCCUGAGCUAUGCUGUUCUCCA	6051
AD-1948026	ccugagCfuAfUfGfcuguucuccu	3090	PaGfgadGa(Agn)cagcauAfgCfucaggaa	4571	UUCCUGAGCUAUGCUGUUCUCCA	6052
AD-1948027	cugagcuaUfGfCfuguucuccau	3091	PadTggdAgdAacagdCaUfagcucagga	4572	UCCUGAGCUAUGCUGUUCUCCAU	6053
AD-1948028	cugagcUfaUfGfCfuguucuccau	3092	PaUfggdAg(Agn)acagcaUfaGfcucagga	4573	UCCUGAGCUAUGCUGUUCUCCAU	6054
AD-1948029	auuuacauCfUfGfuguugucagu	3093	PadCugdAcdAacacdAgAfuguaaaugg	4574	CCAUUUACAUCUGUGUUGUCAGC	6055
AD-1948030	uuuacaucUfGfUfguugucagcu	3094	PadGcudGadCaacadCaGfauguaaaug	4575	CAUUUACAUCUGUGUUGUCAGCA	6056
AD-1948031	uuacaucuGfUfGfuugucagcau	3095	PadTgcdTgdAcaacdAcAfgauguaaau	4576	AUUUACAUCUGUGUUGUCAGCAG	6057
AD-1948032	uuacauCfuGfUfGfuugucagcau	3096	PaUfgcdTg(Agn)caacacAfgAfuguaaau	4577	AUUUACAUCUGUGUUGUCAGCAG	6058
AD-1948033	uacaucugUfGfUfugucagcagu	3097	PadCugdCudGacaadCaCfagauguaaa	4578	UUUACAUCUGUGUUGUCAGCAGA	6059
AD-1948034	acaucuguGfUfUfgucagcagau	3098	PadTcudGcdTgacadAcAfcagauguaa	4579	UUACAUCUGUGUUGUCAGCAGAC	6060
AD-1948035	acaucuGfuGfUfUfgucagcagau	3099	PaUfcudGc(Tgn)gacaacAfcAfgauguaa	4580	UUACAUCUGUGUUGUCAGCAGAC	6061
AD-1948036	uauuucccAfAfAfgcaaauucau	3100	PadTgadAudTugcudTuGfggaaauagg	4581	CCUAUUUCCCAAAGCAAAUUCAA	6062

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948037	uauuucCfcAfAfAfgcaaauucau	3101	PaUfgadAu(Tgn)ugcuuuGfgGfaaauagg	4582	CCUAUUUCCCAAAGCAAAUUCAA	6063
AD-1948038	auuucccaAfAfGfcaaauucaau	3102	PadTugdAadTuugcdTuUfgggaaauag	4583	CUAUUUCCCAAAGCAAAUUCAAG	6064
AD-1948039	uuucccaaAfGfCfaaauucaagu	3103	PadCuudGadAuuugdCuUfugggaaaua	4584	UAUUUCCCAAAGCAAAUUCAAGG	6065
AD-1948040	uucccaaaGfCfAfaauucaaggu	3104	PadCcudTgdAauuudGcUfuugggaaau	4585	AUUUCCCAAAGCAAAUUCAAGGA	6066
AD-1948041	ucccaaagCfAfAfaaucaaggau	3105	PadTccdTudGaauudTgCfuuugggaaa	4586	UUUCCCAAAGCAAAUUCAAGGAA	6067
AD-1948042	cccaaagcAfAfAfuucaaggaau	3106	PadTucdCudTgaaudTuGfcuuugggaa	4587	UUCCCAAAGCAAAUUCAAGGAAA	6068
AD-1948043	cccaaaGfcAfAfAfuucaaggaau	3107	PaUfucdCu(Tgn)gaauuuGfcUfuugggaa	4588	UUCCCAAAGCAAAUUCAAGGAAA	6069
AD-1948044	ccaaagcaAfAfUfucaaggaaau	3108	PadTuudCcdTugaadTuUfgcuuuggga	4589	UCCCAAAGCAAAUUCAAGGAAAA	6070
AD-1948045	ccaaagCfaAfAfUfucaaggaaau	3109	PaUfuudCc(Tgn)ugaauuUfgCfuuuggga	4590	UCCCAAAGCAAAUUCAAGGAAAA	6071
AD-1948046	caaagcaaAfUfUfcaaggaaaau	3110	PadTuudTcdCuugadAuUfugcuuuggg	4591	CCCAAAGCAAAUUCAAGGAAAAA	6072
AD-1948047	aaagcaaaUfUfCfaaggaaaaau	3111	PadTuudTudCcuugdAaUfuugcuuugg	4592	CCAAAGCAAAUUCAAGGAAAAAA	6073
AD-1948048	aagcaaauUfCfAfaggaaaaau	3112	PadTuudTudTccuudGaAfuuugcuuug	4593	CAAAGCAAAUUCAAGGAAAAAAC	6074
AD-1948049	aagcaaAfuUfCfAfaggaaaaaau	3113	PaUfuudTu(Tgn)ccuugaAfuUfugcuuug	4594	CAAAGCAAAUUCAAGGAAAAAAC	6075
AD-1948050	agcaaauuCfAfAfggaaaaacu	3114	PadGuudTudTuccudTgAfauuugcuuu	4595	AAAGCAAAUUCAAGGAAAAAACA	6076
AD-1948051	agcaaaUfuCfAfAfggaaaaaacu	3115	PaGfuudTu(Tgn)uccuugAfaUfuugcuuu	4596	AAAGCAAAUUCAAGGAAAAAACA	6077
AD-1948052	gcaaauucAfAfGfgaaaaaacau	3116	PadTgudTudTuuccdTuGfaauuugcuu	4597	AAGCAAAUUCAAGGAAAAAACAG	6078
AD-1948053	gcaaauUfcAfAfGfgaaaaaacau	3117	PaUfgudTu(Tgn)uuccuuGfaAfuuugcuu	4598	AAGCAAAUUCAAGGAAAAAACAG	6079
AD-1948054	caaauucaAfGfGfaaaaacagu	3118	PadCugdTudTuuucdCuUfgaauuugcu	4599	AGCAAAUUCAAGGAAAAAACAGG	6080
AD-1948055	aaauucaaGfGfAfaaaaacaggu	3119	PadCcudGudTuuuudCcUfugaauuugc	4600	GCAAAUUCAAGGAAAAAACAGGU	6081
AD-1948056	aauucaagGfAfAfaaaacagguu	3120	PadAccdTgdTuuuudTcCfuugaauuug	4601	CAAAUUCAAGGAAAAAACAGGUG	6082
AD-1948057	aauucaAfgGfAfAfaaaacagguu	3121	PaAfccdTg(Tgn)uuuuucCfuUfgaauuug	4602	CAAAUUCAAGGAAAAAACAGGUG	6083
AD-1948058	auucaaggAfAfAfaaacaggugu	3122	PadCacdCudGuuuudTuCfcuugaauuu	4603	AAAUUCAAGGAAAAAACAGGUGA	6084
AD-1948059	uucaaggaAfAfAfaacaggugau	3123	PadTcadCcdTguuudTuUfccuugaauu	4604	AAUUCAAGGAAAAAACAGGUGAU	6085
AD-1948060	uucaagGfaAfAfAfaacaggugau	3124	PaUfcadCc(Tgn)guuuuuUfcCfuugaauu	4605	AAUUCAAGGAAAAAACAGGUGAU	6086

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948061	ucaaggaaAfAfAfAfacaggugauu	3125	PadAucdAcdCuguudTuUfuccuugaau	4606	AUUCAAGGAAAAAACAGGUGAUU	6087
AD-1948062	caaggaaaAfAfAfAfcaggugauuu	3126	PadAaudCadCcugudTuUfuuccuugaa	4607	UUCAAGGAAAAAACAGGUGAUUA	6088
AD-1948063	aaggaaaaAfAfCfaggugauuau	3127	PadTaadTcdAccugdTuUfuuuccuuga	4608	UCAAGGAAAAAACAGGUGAUUAA	6089
AD-1948064	aaggaaAfaAfAfCfaggugauuau	3128	PaUfaadTc(Agn)ccuguuUfuUfuccuuga	4609	UCAAGGAAAAAACAGGUGAUUAA	6090
AD-1948065	aggaaaaaAfCfAfggugauuaau	3129	PadTuadAudCaccudGuUfuuuuccuug	4610	CAAGGAAAAAACAGGUGAUUAAA	6091
AD-1948066	ggaaaaaaCfAfGfgugauuaaau	3130	PadTuudAadTcaccdTgUfuuuuuccuu	4611	AAGGAAAAAACAGGUGAUUAAAG	6092
AD-1948067	ggaaaaAfaCfAfGfgugauuaaau	3131	PaUfuudAa(Tgn)caccugUfuUfuuuccuu	4612	AAGGAAAAAACAGGUGAUUAAAG	6093
AD-1948068	gaaaaaacAfGfGfguauuaaagu	3132	PadCuudTadAucacdCuGfuuuuuuccu	4613	AGGAAAAAACAGGUGAUUAAAGU	6094
AD-1948069	aaaaaacaGfGfUfguuuaaaguu	3133	PadAcudTudAaucadCcUfguuuuuucc	4614	GGAAAAAACAGGUGAUUAAAGUA	6095
AD-1948070	uauacaguGfAfAfgaugaaaccu	3134	PadGgudTudCaucudTcAfcuguauacu	4615	AGUAUACAGUGAAGAUGAAACCA	6096
AD-1948071	auacagugAfAfGfaugaaaccau	3135	PadTggdTudTcaucdTuCfacuguauac	4616	GUAUACAGUGAAGAUGAAACCAG	6097
AD-1948072	auacagUfgAfAfGfaugaaaccau	3136	PaUfggdTu(Tgn)caucuuCfaCfuguauac	4617	GUAUACAGUGAAGAUGAAACCAG	6098
AD-1948073	uacagugaAfGfAfugaaaccagu	3137	PadCugdGudTucaudCuUfcacuguaua	4618	UAUACAGUGAAGAUGAAACCAGC	6099
AD-1948074	gcagggcuUfUfAfgauguacccu	3138	PadGggdTadCaucudAaAfgcccugcug	4619	CAGCAGGGCUUUAGAUGUACCCA	6100
AD-1948075	cagggcuuUfAfGfauguacccau	3139	PadTggdGudAcaucdTaAfagcccugcu	4620	AGCAGGGCUUUAGAUGUACCCAG	6101
AD-1948076	cagggcUfuUfAfGfauguacccau	3140	PaUfggdGu(Agn)caucuaAfaGfcccugcu	4621	AGCAGGGCUUUAGAUGUACCCAG	6102
AD-1948077	agggcuuuAfGfAfuguacccagu	3141	PadCugdGgdTacaudCuAfaagcccugc	4622	GCAGGGCUUUAGAUGUACCCAGU	6103
AD-1948078	agggcuUfuAfGfAfuguacccagu	3142	PaCfugdGg(Tgn)acaucuAfaAfgcccugc	4623	GCAGGGCUUUAGAUGUACCCAGU	6104
AD-1948079	gggcuuuaGfAfUfguacccaguu	3143	PadAcudGgdGuacadTcUfaaagcccug	4624	CAGGGCUUUAGAUGUACCCAGUG	6105
AD-1948080	ggcuuuagAfUfGfuacccagugu	3144	PadCacdTgdGguacdAuCfuaaagcccu	4625	AGGGCUUUAGAUGUACCCAGUGA	6106
AD-1948081	gcuuuagaUfGfUfacccagugau	3145	PadTcadCudGgguadCaUfcuaaagccc	4626	GGGCUUUAGAUGUACCCAGUGAC	6107
AD-1948082	uuuagaugUfAfCfccagugacau	3146	PadTgudCadCugggdTaCfaucuaaagc	4627	GCUUUAGAUGUACCCAGUGACAU	6108
AD-1948083	uuagauguAfCfCfcagugacauu	3147	PadAugdTcdAcuggdGuAfcaucuaaag	4628	CUUUAGAUGUACCCAGUGACAUA	6109
AD-1948084	uuagauGfuAfCfCfcagugacauu	3148	PaAfugdTc(Agn)cuggguAfcAfucuaaag	4629	CUUUAGAUGUACCCAGUGACAUA	6110

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948085	uagauguaCfCfCfagugacauau	3149	PadTaudGudCacugdGgUfacaucuaaa	4630	UUUAGAUGUACCCAGUGACAUAA	6111
AD-1948086	agauguacCfCfAfgugacauaau	3150	PadTuadTgdTcacudGgGfuacaucuaa	4631	UUAGAUGUACCCAGUGACAUAAC	6112
AD-1948087	agauguAfcCfCfAfgugacauaau	3151	PaUfuadTg(Tgn)cacuggGfuAfcaucuaa	4632	UUAGAUGUACCCAGUGACAUAAC	6113
AD-1948088	gauguaccCfAfGfugacauaacu	3152	PadGuudAudGucacdTgGfguacaucua	4633	UAGAUGUACCCAGUGACAUAACG	6114
AD-1948089	uguacccaGfUfGfacauaacggu	3153	PadCcgdTudAugucdAcUfggguacauc	4634	GAUGUACCCAGUGACAUAACGGC	6115
AD-1948090	guacccagUfGfAfcauaacggcu	3154	PadGccdGudTaugudCaCfuggguacau	4635	AUGUACCCAGUGACAUAACGGCU	6116
AD-1948091	uacccaguGfAfCfauaacggcuu	3155	PadAgcdCgdTuaugdTcAfcuggguaca	4636	UGUACCCAGUGACAUAACGGCUC	6117
AD-1948092	acccagugAfCfAfuaacggcucu	3156	PadGagdCcdGuuaudGuCfacuggguac	4637	GUACCCAGUGACAUAACGGCUCG	6118
AD-1948093	ccagugacAfUfAfacggcucgau	3157	PadTcgdAgdCcguudAuGfucacugggu	4638	ACCCAGUGACAUAACGGCUCGAG	6119
AD-1948094	cagugacaUfAfAfcggcucgagu	3158	PadCucdGadGccgudTaUfgucacuggg	4639	CCCAGUGACAUAACGGCUCGAGA	6120
AD-1948095	gugacauaAfCfGfgcucgagauu	3159	PadAucdTcdGagccdGuUfaugucacug	4640	CAGUGACAUAACGGCUCGAGAUG	6121
AD-1948096	ugacauaaCfGfGfcucgagaugu	3160	PadCaudCudCgagcdCgUfuaugucacu	4641	AGUGACAUAACGGCUCGAGAUGU	6122
AD-1948097	gacauaacGfGfCfucgagauguu	3161	PadAcadTcdTcgagdCcGfuuaugucac	4642	GUGACAUAACGGCUCGAGAUGUU	6123
AD-1948098	gacauaAfcGfGfCfucgagauguu	3162	PaAfcadTc(Tgn)cgagccGfuUfaugucac	4643	GUGACAUAACGGCUCGAGAUGUU	6124
AD-1948099	acauaacgGfCfUfcgagauguuu	3163	PadAacdAudCucgadGcCfguuauguca	4644	UGACAUAACGGCUCGAGAUGUUU	6125
AD-1948100	cauaacggCfUfCfgagauguuuu	3164	PadAaadCadTcucgdAgCfcguuauguc	4645	GACAUAACGGCUCGAGAUGUUUG	6126
AD-1948101	cauaacGfgCfUfCfgagauguuuu	3165	PaAfaadCa(Tgn)cucgagCfcGfuuauguc	4646	GACAUAACGGCUCGAGAUGUUUG	6127
AD-1948102	auaacggcUfCfGfagauguuugu	3166	PadCaadAcdAucucdGaGfccguuaugu	4647	ACAUAACGGCUCGAGAUGUUUGU	6128
AD-1948103	uaacggcuCfGfAfgauguuuguu	3167	PadAcadAadCaucudCgAfgccguuaug	4648	CAUAACGGCUCGAGAUGUUUGUC	6129
AD-1948104	aacggcucGfAfGfauguuugucu	3168	PadGacdAadAcaucdTcGfagccguuau	4649	AUAACGGCUCGAGAUGUUUGUCA	6130
AD-1948105	acggcucgAfGfAfuguuugucau	3169	PadTgadCadAacaudCuCfgagccguua	4650	UAACGGCUCGAGAUGUUUGUCAG	6131
AD-1948106	cggcucgaGfAfUfguuugucagu	3170	PadCugdAcdAaacadTcUfcgagccguu	4651	AACGGCUCGAGAUGUUUGUCAGC	6132
AD-1948107	ggcucgagAfUfGfuuugucagcu	3171	PadGcudGadCaaacdAuCfucgagccgu	4652	ACGGCUCGAGAUGUUUGUCAGCU	6133
AD-1948108	gcucgagaUfGfUfuugucagcuu	3172	PadAgcdTgdAcaaadCaUfcucgagccg	4653	CGGCUCGAGAUGUUUGUCAGCUG	6134

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948109	gcucgaGfaUfGfUfuugucagcuu	3173	PaAfgcdTg(Agn)caaacaUfcUfcgagccg	4654	CGGCUCGAGAUGUUUGUCAGCUG	6135
AD-1948110	cucgagauGfUfUfugucagcugu	3174	PadCagdCudGacaadAcAfucucgagcc	4655	GGCUCGAGAUGUUUGUCAGCUGU	6136
AD-1948111	ucgagaugUfUfUfgucagcuguu	3175	PadAcadGcdTgacadAaCfaucucgagc	4656	GCUCGAGAUGUUUGUCAGCUGUU	6137
AD-1948112	ucgagaUfgUfUfUfgucagcuguu	3176	PaAfcadGc(Tgn)gacaaaCfaUfcucgagc	4657	GCUCGAGAUGUUUGUCAGCUGUU	6138
AD-1948113	cgagauguUfUfGfucagcuguuu	3177	PadAacdAgdCugacdAaAfcaucucgag	4658	CUCGAGAUGUUUGUCAGCUGUUG	6139
AD-1948114	gagauguuUfGfUfcagcuguugu	3178	PadCaadCadGcugadCaAfacaucucga	4659	UCGAGAUGUUUGUCAGCUGUUGA	6140
AD-1948115	agauguuuGfUfCfagcuguugau	3179	PadTcadAcdAgcugdAcAfaacaucucg	4660	CGAGAUGUUUGUCAGCUGUUGAU	6141
AD-1948116	agauguUfuGfUfCfagcuguugau	3180	PaUfcadAc(Agn)gcugacAfaAfcaucucg	4661	CGAGAUGUUUGUCAGCUGUUGAU	6142
AD-1948117	gauguuugUfCfAfgcuguugauu	3181	PadAucdAadCagcudGaCfaaacaucuc	4662	GAGAUGUUUGUCAGCUGUUGAUC	6143
AD-1948118	auguuuguCfAfGfcuguugaucu	3182	PadGaudCadAcagcdTgAfcaaacaucu	4663	AGAUGUUUGUCAGCUGUUGAUCC	6144
AD-1948119	auguuuGfuCfAfGfcuguugaucu	3183	PaGfaudCa(Agn)cagcugAfcAfaacaucu	4664	AGAUGUUUGUCAGCUGUUGAUCC	6145
AD-1948120	uguuugucAfGfCfuguugauccu	3184	PadGgadTcdAacagdCuGfacaaacauc	4665	GAUGUUUGUCAGCUGUUGAUCCU	6146
AD-1948121	uguuugUfcAfGfCfuguugauccu	3185	PaGfgadTc(Agn)acagcuGfaCfaaacauc	4666	GAUGUUUGUCAGCUGUUGAUCCU	6147
AD-1948122	guuugucaGfCfUfguugauccuu	3186	PadAggdAudCaacadGcUfgacaaacau	4667	AUGUUUGUCAGCUGUUGAUCCUG	6148
AD-1948123	uuugucagCfUfGfuugauccugu	3187	PadCagdGadTcaacdAgCfugacaaaca	4668	UGUUUGUCAGCUGUUGAUCCUGA	6149
AD-1948124	uugucagcUfGfUfugauccugau	3188	PadTcadGgdAucaadCaGfcugacaaac	4669	GUUUGUCAGCUGUUGAUCCUGAA	6150
AD-1948125	uugucaGfcUfGfUfugauccugau	3189	PaUfcadGg(Agn)ucaacaGfcUfgacaaac	4670	GUUUGUCAGCUGUUGAUCCUGAA	6151
AD-1948126	ugucagcuGfUfUfgauccugaau	3190	PadTucdAgdGaucadAcAfgcugacaaa	4671	UUUGUCAGCUGUUGAUCCUGAAG	6152
AD-1948127	gucagcugUfUfGfauccugaagu	3191	PadCuudCadGgaucdAaCfagcugacaa	4672	UUGUCAGCUGUUGAUCCUGAAGA	6153
AD-1948128	ucagcuguUfGfAfuccugaagau	3192	PadTcudTcdAggaudCaAfcagcugaca	4673	UGUCAGCUGUUGAUCCUGAAGAA	6154
AD-1948129	ucagcuGfuUfGfAfuccugaagau	3193	PaUfcudTc(Agn)ggaucaAfcAfgcugaca	4674	UGUCAGCUGUUGAUCCUGAAGAA	6155
AD-1948130	cagcuguuGfAfUfccugaagaau	3194	PadTucdTudCaggadTcAfacagcugac	4675	GUCAGCUGUUGAUCCUGAAGAAU	6156
AD-1948131	agcuguugAfUfCfcugaagaauu	3195	PadAuudCudTcaggdAuCfaacagcuga	4676	UCAGCUGUUGAUCCUGAAGAAUC	6157
AD-1948132	agcuguUfgAfUfCfcugaagaauu	3196	PaAfuudCu(Tgn)caggauCfaAfcagcuga	4677	UCAGCUGUUGAUCCUGAAGAAUC	6158

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948133	gcuguugaUfCfCfugaagaaucu	3197	PadGaudTcdTucagdGaUfcaacagcug	4678	CAGCUGUUGAUCCUGAAGAAUCA	6159
AD-1948134	gcuguuGfaUfCfCfugaagaaucu	3198	PaGfaudTc(Tgn)ucaggaUfcAfacagcug	4679	CAGCUGUUGAUCCUGAAGAAUCA	6160
AD-1948135	cuguugauCfCfUfgaagaaucau	3199	PadTgadTudCuucadGgAfucaacagcu	4680	AGCUGUUGAUCCUGAAGAAUCAU	6161
AD-1948136	uguugaucCfUfGfaagaaucauu	3200	PadAugdAudTcuucdAgGfaucaacagc	4681	GCUGUUGAUCCUGAAGAAUCAUU	6162
AD-1948137	guugauccUfGfAfagaaucauuu	3201	PadAaudGadTucuudCaGfgaucaacag	4682	CUGUUGAUCCUGAAGAAUCAUUA	6163
AD-1948138	guugauCfcUfGfAfagaaucauuu	3202	PaAfaudGa(Tgn)ucuucaGfgAfucaacag	4683	CUGUUGAUCCUGAAGAAUCAUUA	6164
AD-1948139	uugauccuGfAfAfgaaucauuau	3203	PadTaadTgdAuucudTcAfggaucaaca	4684	UGUUGAUCCUGAAGAAUCAUUAC	6165
AD-1948140	uugaucCfuGfAfAfgaaucauuau	3204	PaUfaadTg(Agn)uucuucAfgGfaucaaca	4685	UGUUGAUCCUGAAGAAUCAUUAC	6166
AD-1948141	ugauccugAfAfGfaaucauuacu	3205	PadGuadAudGauucdTuCfaggaucaac	4686	GUUGAUCCUGAAGAAUCAUUACA	6167
AD-1948142	gauccugaAfGfAfaucauuacau	3206	PadTgudAadTgauudCuUfcaggaucaa	4687	UUGAUCCUGAAGAAUCAUUACAU	6168
AD-1948143	cccuuuuuGfAfGfcaccugccuu	3207	PadAggdCadGgugcdTcAfaaaaggguc	4688	GACCCUUUUUGAGCACCUGCCUC	6169
AD-1948144	ccuuuuugAfGfCfaccugccucu	3208	PadGagdGcdAggugdCuCfaaaaagggu	4689	ACCCUUUUUGAGCACCUGCCUCA	6170
AD-1948145	ccuuuuUfgAfGfCfaccugccucu	3209	PaGfagdGc(Agn)ggugcuCfaAfaaagggu	4690	ACCCUUUUUGAGCACCUGCCUCA	6171
AD-1948146	cuuuuugaGfCfAfccugccucau	3210	PadTgadGgdCaggudGcUfcaaaaaggg	4691	CCCUUUUUGAGCACCUGCCUCAC	6172
AD-1948147	gagcaccuGfCfCfucacauaggu	3211	PadCcudAudGugagdGcAfggugcucaa	4692	UUGAGCACCUGCCUCACAUAGGU	6173
AD-1948148	caccugccUfCfAfcauagguguu	3212	PadAcadCcdTaugudGaGfgcaggugcu	4693	AGCACCUGCCUCACAUAGGUGUA	6174
AD-1948149	gccucacaUfAfGfguguagaaau	3213	PadTuudCudAcaccdTaUfgugaggcag	4694	CUGCCUCACAUAGGUGUAGAAAG	6175
AD-1948150	gccucaCfaUfAfGfguguagaaau	3214	PaUfuudCu(Agn)caccuaUfgUfgaggcag	4695	CUGCCUCACAUAGGUGUAGAAAG	6176
AD-1948151	ccucacauAfGfGfuguagaaagu	3215	PadCuudTcdTacacdCuAfugugaggca	4696	UGCCUCACAUAGGUGUAGAAAGA	6177
AD-1948152	ccucacAfuAfGfGfuguagaaagu	3216	PaCfuudTc(Tgn)acaccuAfuGfugaggca	4697	UGCCUCACAUAGGUGUAGAAAGA	6178
AD-1948153	cucacauaGfGfUfguagaaagau	3217	PadTcudTudCuacadCcUfaugugaggc	4698	GCCUCACAUAGGUGUAGAAAGAA	6179
AD-1948154	ucacauagGfUfGfuagaaagaau	3218	PadTucdTudTcuacdAcCfuaugugagg	4699	CCUCACAUAGGUGUAGAAAGAAC	6180
AD-1948155	ucacauAfgGfUfGfuagaaagaau	3219	PaUfucdTu(Tgn)cuacacCfuAfugugagg	4700	CCUCACAUAGGUGUAGAAAGAAC	6181
AD-1948156	cacauaggUfGfUfagaaagaacu	3220	PadGuudCudTucuadCaCfcuaugugag	4701	CUCACAUAGGUGUAGAAAGAACA	6182

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948157	cacauaGfgUfGfUfagaaagaacu	3221	PaGfuudCu(Tgn)ucuacaCfcUfaugugag	4702	CUCACAUAGGUGUAGAAAGAACA	6183
AD-1948158	acauagguGfUfAfgaaagaacau	3222	PadTgudTcdTuucudAcAfccuauguga	4703	UCACAUAGGUGUAGAAAGAACAA	6184
AD-1948159	acauagGfuGfUfAfgaaagaacau	3223	PaUfgudTc(Tgn)uucuacAfcCfuauguga	4704	UCACAUAGGUGUAGAAAGAACAA	6185
AD-1948160	cauaggugUfAfGfaaagaacaau	3224	PadTugdTudCuuucdTaCfaccuaugug	4705	CACAUAGGUGUAGAAAGAACAAU	6186
AD-1948161	auagguguAfGfAfaagaacaauu	3225	PadAuudGudTcuuudCuAfcaccuaugu	4706	ACAUAGGUGUAGAAAGAACAAUA	6187
AD-1948162	auagguGfuAfGfAfaagaacaauu	3226	PaAfuudGu(Tgn)cuuucuAfcAfccuaugu	4707	ACAUAGGUGUAGAAAGAACAAUA	6188
AD-1948163	uagguguaGfAfAfagaacaauau	3227	PadTaudTgdTucuudTcUfacaccuaug	4708	CAUAGGUGUAGAAAGAACAAUAG	6189
AD-1948164	uaggugUfaGfAfAfagaacaauau	3228	PaUfaudTg(Tgn)ucuuucUfaCfaccuaug	4709	CAUAGGUGUAGAAAGAACAAUAG	6190
AD-1948165	agguguagAfAfAfgaacaauagu	3229	PadCuadTudGuucudTuCfuacaccuau	4710	AUAGGUGUAGAAAGAACAAUAGA	6191
AD-1948166	gguguagaAfAfGfaacaauagau	3230	PadTcudAudTguucdTuUfcuacaccua	4711	UAGGUGUAGAAAGAACAAUAGAA	6192
AD-1948167	guguagaaAfGfAfacaauagaau	3231	PadTucdTadTuguudCuUfucuacaccu	4712	AGGUGUAGAAAGAACAAUAGAAG	6193
AD-1948168	guguagAfaAfGfAfacaauagaau	3232	PaUfucdTa(Tgn)uguucuUfuCfuacaccu	4713	AGGUGUAGAAAGAACAAUAGAAG	6194
AD-1948169	uguagaaaGfAfAfcaauagaagu	3233	PadCuudCudAuugudTcUfuucuacacc	4714	GGUGUAGAAAGAACAAUAGAAGA	6195
AD-1948170	guagaaagAfAfCfaauagaagau	3234	PadTcudTcdTauugdTuCfuuucuacac	4715	GUGUAGAAAGAACAAUAGAAGAC	6196
AD-1948171	guagaaAfgAfAfCfaauagaagau	3235	PaUfcudTc(Tgn)auuguuCfuUfucuacac	4716	GUGUAGAAAGAACAAUAGAAGAC	6197
AD-1948172	uagaaagaAfCfAfauagaagacu	3236	PadGucdTudCuauudGuUfcuuucuaca	4717	UGUAGAAAGAACAAUAGAAGACC	6198
AD-1948173	agaaagaaCfAfAfuagaagaccu	3237	PadGgudCudTcuaudTgUfucuuucuac	4718	GUAGAAAGAACAAUAGAAGACCA	6199
AD-1948174	agaaagAfaCfAfAfuagaagaccu	3238	PaGfgudCu(Tgn)cuauugUfuCfuuucuac	4719	GUAGAAAGAACAAUAGAAGACCA	6200
AD-1948175	gaaagaacAfAfUfagaagaccau	3239	PadTggdTcdTucuadTuGfuucuuucua	4720	UAGAAAGAACAAUAGAAGACCAC	6201
AD-1948176	gaaagaAfcAfAfUfagaagaccau	3240	PaUfggdTc(Tgn)ucuauuGfuUfcuuucua	4721	UAGAAAGAACAAUAGAAGACCAC	6202
AD-1948177	acgaacugGfUfGfauugaagugu	3241	PadCacdTudCaaucdAcCfaguucgugg	4722	CCACGAACUGGUGAUUGAAGUGC	6203
AD-1948178	cgaacuggUfGfAfuugaagugcu	3242	PadGcadCudTcaaudCaCfcaguucgug	4723	CACGAACUGGUGAUUGAAGUGCU	6204
AD-1948179	cgaacuGfgUfGfAfuugaagugcu	3243	PaGfcadCu(Tgn)caaucaCfcAfguucgug	4724	CACGAACUGGUGAUUGAAGUGCU	6205
AD-1948180	gaacugguGfAfUfugaagugcuu	3244	PadAgcdAcdTucaadTcAfccaguucgu	4725	ACGAACUGGUGAUUGAAGUGCUA	6206

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948181	gaacugGfuGfAfUfugaagugcuu	3245	PaAfgcdAc(Tgn)ucaaucAfcCfaguucgu	4726	ACGAACUGGUGAUUGAAGUGCUA	6207
AD-1948182	aacuggugAfUfUfggaagugcuau	3246	PadTagdCadCuucadAuCfaccaguucg	4727	CGAACUGGUGAUUGAAGUGCUAU	6208
AD-1948183	acuggugaUfUfGfaagugcuauu	3247	PadAuadGcdAcuucdAaUfcaccaguuc	4728	GAACUGGUGAUUGAAGUGCUAUC	6209
AD-1948184	acugguGfaUfUfGfaagugcuauu	3248	PaAfuadGc(Agn)cuucaaUfcAfccaguuc	4729	GAACUGGUGAUUGAAGUGCUAUC	6210
AD-1948185	cuggugauUfGfAfagugcuaucu	3249	PadGaudAgdCacuudCaAfucaccaguu	4730	AACUGGUGAUUGAAGUGCUAUCC	6211
AD-1948186	uggugauuGfAfAfgugcuauccu	3250	PadGgadTadGcacudTcAfaucaccagu	4731	ACUGGUGAUUGAAGUGCUAUCCA	6212
AD-1948187	ggugauugAfAfGfugcuauccau	3251	PadTggdAudAgcacdTuCfaaucaccag	4732	CUGGUGAUUGAAGUGCUAUCCAA	6213
AD-1948188	ggugauUfgAfAfGfugcuauccau	3252	PaUfggdAu(Agn)gcacuuCfaAfucaccag	4733	CUGGUGAUUGAAGUGCUAUCCAA	6214
AD-1948189	gugauugaAfGfUfgcuauccaau	3253	PadTugdGadTagcadCuUfcaaucacca	4734	UGGUGAUUGAAGUGCUAUCCAAC	6215
AD-1948190	gugauuGfaAfGfUfgcuauccaau	3254	PaUfugdGa(Tgn)agcacuUfcAfaucacca	4735	UGGUGAUUGAAGUGCUAUCCAAC	6216
AD-1948191	ugauugaaGfUfGfcuauccaacu	3255	PadGuudGgdAuagcdAcUfucaaucacc	4736	GGUGAUUGAAGUGCUAUCCAACU	6217
AD-1948192	ugauugAfaGfUfGfcuauccaacu	3256	PaGfuudGg(Agn)uagcacUfuCfaaucacc	4737	GGUGAUUGAAGUGCUAUCCAACU	6218
AD-1948193	gauugaagUfGfCfuauccaacuu	3257	PadAgudTgdGauagdCaCfuucaaucac	4738	GUGAUUGAAGUGCUAUCCAACUG	6219
AD-1948194	auugaaguGfCfUfauccaacugu	3258	PadCagdTudGgauadGcAfcuucaauca	4739	UGAUUGAAGUGCUAUCCAACUGG	6220
AD-1948195	uugaagugCfUfAfuccaacuggu	3259	PadCcadGudTggaudAgCfacuucaauc	4740	GAUUGAAGUGCUAUCCAACUGGG	6221
AD-1948196	aaaaauuaUfGfCfcaaauaugau	3260	PadTcadTadTuuggdCaUfaauuuuuuc	4741	GAAAAAAUUAUGCCAAAUAUGAG	6222
AD-1948197	aauuaugcCfAfAfauaugaguuu	3261	PadAacdTcdAuauudTgGfcauaauuuu	4742	AAAAUUAUGCCAAAUAUGAGUUC	6223
AD-1948198	aauuauGfcCfAfAfauaugaguuu	3262	PaAfacdTc(Agn)uauuugGfcAfuaauuuu	4743	AAAAUUAUGCCAAAUAUGAGUUC	6224
AD-1948199	auuaugccAfAfAfuaugaguucu	3263	PadGaadCudCauaudTuGfgcauaauuu	4744	AAAUUAUGCCAAAUAUGAGUUCU	6225
AD-1948200	uuaugccaAfAfUfaugaguucuu	3264	PadAgadAcdTcauadTuUfggcauaauu	4745	AAUUAUGCCAAAUAUGAGUUCUU	6226
AD-1948201	uuaugcCfaAfAfUfaugaguucuu	3265	PaAfgadAc(Tgn)cauauuUfgGfcauaauu	4746	AAUUAUGCCAAAUAUGAGUUCUU	6227
AD-1948202	uaugccaaAfUfAfugaguucuuu	3266	PadAagdAadCucaudAuUfuggcauaau	4747	AUUAUGCCAAAUAUGAGUUCUUU	6228
AD-1948203	augccaaaUfAfUfgaguucuuuu	3267	PadAaadGadAcucadTaUfuuggcauaa	4748	UUAUGCCAAAUAUGAGUUCUUUA	6229
AD-1948204	augccaAfaUfAfUfgaguucuuuu	3268	PaAfaadGa(Agn)cucauaUfuUfggcauaa	4749	UUAUGCCAAAUAUGAGUUCUUUA	6230

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948205	ugccaaauAfUfGfaguucuuuau	3269	PadTaadAgdAacucdAuAfuuuggcaua	4750	UAUGCCAAAUAUGAGUUCUUUAA	6231
AD-1948206	gccaaauaUfGfAfguucuuuaau	3270	PadTuadAadGaacudCaUfauuuggcau	4751	AUGCCAAAUAUGAGUUCUUUAAA	6232
AD-1948207	ccaaauauGfAfGfuucuuuaaau	3271	PadTuudAadAgaacdTcAfuauuuggca	4752	UGCCAAAUAUGAGUUCUUUAAAA	6233
AD-1948208	caaauaugAfGfUfucuuuaaaau	3272	PadTuudTadAagaadCuCfauauuuggc	4753	GCCAAAUAUGAGUUCUUUAAAAA	6234
AD-1948209	aaauaugaGfUfUfcuuuaaaaau	3273	PadTuudTudAaagadAcUfcauauuugg	4754	CCAAAUAUGAGUUCUUUAAAAAC	6235
AD-1948210	aauaugagUfUfCfuuuaaaaacu	3274	PadGuudTudTaaagdAaCfucauauuug	4755	CAAAUAUGAGUUCUUUAAAAACC	6236
AD-1948211	aauaugAfgUfUfCfuuuaaaaacu	3275	PaGfuudTu(Tgn)aaagaaCfuCfauauuug	4756	CAAAUAUGAGUUCUUUAAAAACC	6237
AD-1948212	auaugaguUfCfUfuuaaaaaccu	3276	PadGgudTudTuaaadGaAfcucauauuu	4757	AAAUAUGAGUUCUUUAAAAACCC	6238
AD-1948213	auaugaGfuUfCfUfuuaaaaaccu	3277	PaGfgudTu(Tgn)uaaagaAfcUfcauauuu	4758	AAAUAUGAGUUCUUUAAAAACCC	6239
AD-1948214	uaugaguuCfUfUfuaaaaacccu	3278	PadGggdTudTuuaadAgAfacucauauu	4759	AAUAUGAGUUCUUUAAAAACCCA	6240
AD-1948215	uaugagUfuCfUfUfuaaaaacccu	3279	PaGfggdTu(Tgn)uuaaagAfaCfucauauu	4760	AAUAUGAGUUCUUUAAAAACCCA	6241
AD-1948216	augaguucUfUfUfaaaaacccau	3280	PadTggdGudTuuuadAaGfaacucauau	4761	AUAUGAGUUCUUUAAAAACCCAA	6242
AD-1948217	augaguUfcUfUfUfaaaaacccau	3281	PaUfggdGu(Tgn)uuuaaaGfaAfcucauau	4762	AUAUGAGUUCUUUAAAAACCCAA	6243
AD-1948218	ugaguucuUfUfAfaaaacccaau	3282	PadTugdGgdTuuuudAaAfgaacucaua	4763	UAUGAGUUCUUUAAAAACCCAAU	6244
AD-1948219	ugaguuCfuUfUfAfaaaacccaau	3283	PaUfugdGg(Tgn)uuuuaaAfgAfacucaua	4764	UAUGAGUUCUUUAAAAACCCAAU	6245
AD-1948220	gaguucuuUfAfAfaaacccaauu	3284	PadAuudGgdGuuuudTaAfagaacucau	4765	AUGAGUUCUUUAAAAACCCAAUG	6246
AD-1948221	aguucuuuAfAfAfaacccaaugu	3285	PadCaudTgdGguuudTuAfaagaacuca	4766	UGAGUUCUUUAAAAACCCAAUGU	6247
AD-1948222	guucuuuaAfAfAfacccaauguu	3286	PadAcadTudGgguudTuUfaaagaacuc	4767	GAGUUCUUUAAAAACCCAAUGUA	6248
AD-1948223	uucuuuaaAfAfAfcccaauguau	3287	PadTacdAudTgggudTuUfuaaagaacu	4768	AGUUCUUUAAAAACCCAAUGUAU	6249
AD-1948224	ucuuuaaaAfAfCfccaauguauu	3288	PadAuadCadTugggdTuUfuuaaagaac	4769	GUUCUUUAAAAACCCAAUGUAUU	6250
AD-1948225	aaacccaaUfGfUfauuuuuucu	3289	PadGaadAadAaauadCaUfuggguuuuu	4770	AAAAACCCAAUGUAUUUUUUUCC	6251
AD-1948226	aacccaauGfUfAfuuuuuuccu	3290	PadGgadAadAaaaudAcAfuuggguuuu	4771	AAAACCCAAUGUAUUUUUUUCCA	6252
AD-1948227	acccaaugUfAfUfuuuuuccau	3291	PadTggdAadAaaaadTaCfauuggguuu	4772	AAACCCAAUGUAUUUUUUUCCAG	6253
AD-1948228	cccaauguAfUfUfuuuuccagu	3292	PadCugdGadAaaaadAuAfcauuggguu	4773	AACCCAAUGUAUUUUUUUCCAGA	6254

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948229	ccaauguaUfUfUfuuuuccagau	3293	PadTcudGgdAaaaadAaUfacauugggu	4774	ACCCAAUGUAUUUUUUUCCAGAG	6255
AD-1948230	ccaaugUfaUfUfUfuuuuccagau	3294	PaUfcudGg(Agn)aaaaaaUfaCfauugggu	4775	ACCCAAUGUAUUUUUUUCCAGAG	6256
AD-1948231	caauguauUfUfUfuuuccagagu	3295	PadCucdTgdGaaaadAaAfuacauuggg	4776	CCCAAUGUAUUUUUUUCCAGAGC	6257
AD-1948232	aauguauuUfUfUfuuccagagcu	3296	PadGcudCudGgaaadAaAfauacauugg	4777	CCAAUGUAUUUUUUUCCAGAGCA	6258
AD-1948233	auguauuuUfUfUfuccagagcau	3297	PadTgcdTcdTggaadAaAfaauacauug	4778	CAAUGUAUUUUUUUCCAGAGCAU	6259
AD-1948234	auguauUfuUfUfUfuccagagcau	3298	PaUfgcdTc(Tgn)ggaaaaAfaAfuacauug	4779	CAAUGUAUUUUUUUCCAGAGCAU	6260
AD-1948235	uguauuuuUfUfUfccagagcauu	3299	PadAugdCudCuggadAaAfaaauacauu	4780	AAUGUAUUUUUUUCCAGAGCAUA	6261
AD-1948236	guauuuuUfUfCfcagagcauau	3300	PadTaudGcdTcuggdAaAfaaaauacau	4781	AUGUAUUUUUUUCCAGAGCAUAU	6262
AD-1948237	guauuUfuUfUfCfcagagcauau	3301	PaUfaudGc(Tgn)cuggaaAfaAfaauacau	4782	AUGUAUUUUUUUCCAGAGCAUAU	6263
AD-1948238	uauuuuuuUfCfCfagagcauauu	3302	PadAuadTgdCucugdGaAfaaaaauaca	4783	UGUAUUUUUUUCCAGAGCAUAUG	6264
AD-1948239	auuuuuuuCfCfAfgagcauaugu	3303	PadCaudAudGcucudGgAfaaaaaauac	4784	GUAUUUUUUUCCAGAGCAUAUGG	6265
AD-1948240	uuuuuuucCfAfGfagcauauggu	3304	PadCcadTadTgcucdTgGfaaaaaaaua	4785	UAUUUUUUUCCAGAGCAUAUGGU	6266
AD-1948241	uuuuuuccAfGfAfgcauaugguu	3305	PadAccdAudAugcudCuGfgaaaaaaau	4786	AUUUUUUUCCAGAGCAUAUGGUA	6267
AD-1948242	uuuuuccaGfAfGfcauaugguau	3306	PadTacdCadTaugcdTcUfggaaaaaaa	4787	UUUUUUUCCAGAGCAUAUGGUAU	6268
AD-1948243	uuuuccagAfGfCfauaugguauu	3307	PadAuadCcdAuaugdCuCfuggaaaaaa	4788	UUUUUUCCAGAGCAUAUGGUAUC	6269
AD-1948244	uuuuccAfgAfGfCfauaugguauu	3308	PaAfuadCc(Agn)uaugcuCfuGfgaaaaaa	4789	UUUUUUCCAGAGCAUAUGGUAUC	6270
AD-1948245	uuuccagaGfCfAfuaugguaucu	3309	PadGaudAcdCauaudGcUfcuggaaaaa	4790	UUUUUCCAGAGCAUAUGGUAUCU	6271
AD-1948246	uuccagagCfAfUfaugguaucuu	3310	PadAgadTadCcauadTgCfucuggaaaa	4791	UUUUCCAGAGCAUAUGGUAUCUU	6272
AD-1948247	uccagagcAfUfAfugguaucuuu	3311	PadAagdAudAccaudAuGfcucuggaaa	4792	UUUCCAGAGCAUAUGGUAUCUUU	6273
AD-1948248	ccagagcaUfAfUfgguaucuuuu	3312	PadAaadGadTaccadTaUfgcucuggaa	4793	UUCCAGAGCAUAUGGUAUCUUUU	6274
AD-1948249	ccagagCfaUfAfUfgguaucuuuu	3313	PaAfaadGa(Tgn)accauaUfgCfucuggaa	4794	UUCCAGAGCAUAUGGUAUCUUUU	6275
AD-1948250	cagagcauAfUfGfguaucuuuuu	3314	PadAaadAgdAuaccdAuAfugcucugga	4795	UCCAGAGCAUAUGGUAUCUUUUG	6276
AD-1948251	cagagcAfuAfUfGfguaucuuuuu	3315	PaAfaadAg(Agn)uaccauAfuGfcucugga	4796	UCCAGAGCAUAUGGUAUCUUUUG	6277
AD-1948252	agagcauaUfGfGfuaucuuuugu	3316	PadCaadAadGauacdCaUfaugcucugg	4797	CCAGAGCAUAUGGUAUCUUUUGC	6278

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948253	gagcauauGfGfUfaucuuuugcu	3317	PadGcadAadAgauadCcAfuaugcucug	4798	CAGAGCAUAUGGUAUCUUUUGCA	6279
AD-1948254	agcauaugGfUfAfucuuuugcau	3318	PadTgcdAadAagaudAcCfauaugcucu	4799	AGAGCAUAUGGUAUCUUUUGCAA	6280
AD-1948255	gcauauggUfAfUfcuuuugcaau	3319	PadTugdCadAaagadTaCfcauaugcuc	4800	GAGCAUAUGGUAUCUUUUGCAAC	6281
AD-1948256	cauaugguAfUfCfuuuugcaacu	3320	PadGuudGcdAaaagdAuAfccauaugcu	4801	AGCAUAUGGUAUCUUUUGCAACU	6282
AD-1948257	cauaugGfuAfUfCfuuuugcaacu	3321	PaGfuudGc(Agn)aaagauAfcCfauaugcu	4802	AGCAUAUGGUAUCUUUUGCAACU	6283
AD-1948258	auaugguaUfCfUfuuugcaacuu	3322	PadAgudTgdCaaaadGaUfaccauaugc	4803	GCAUAUGGUAUCUUUUGCAACUG	6284
AD-1948259	uaugguauCfUfUfugcaacugu	3323	PadCagdTudGcaaadAgAfuaccauaug	4804	CAUAUGGUAUCUUUUGCAACUGA	6285
AD-1948260	augguaucUfUfUfugcaacugau	3324	PadTcadGudTgcaadAaGfauaccauau	4805	AUAUGGUAUCUUUUGCAACUGAA	6286
AD-1948261	augguaUfcUfUfUfugcaacugau	3325	PaUfcadGu(Tgn)gcaaaaGfaUfaccauau	4806	AUAUGGUAUCUUUUGCAACUGAA	6287
AD-1948262	ugguaucuUfUfUfgcaacugaau	3326	PadTucdAgdTugcadAaAfgauaccaua	4807	UAUGGUAUCUUUUGCAACUGAAA	6288
AD-1948263	ugguauCfuUfUfUfgcaacugaau	3327	PaUfucdAg(Tgn)ugcaaaAfgAfuaccaua	4808	UAUGGUAUCUUUUGCAACUGAAA	6289
AD-1948264	gguaucuuUfUfGfcaacugaaau	3328	PadTuudCadGuugcdAaAfagauaccau	4809	AUGGUAUCUUUUGCAACUGAAAC	6290
AD-1948265	guaucuuuUfGfCfaacugaaacu	3329	PadGuudTcdAguugdCaAfaagauacca	4810	UGGUAUCUUUUGCAACUGAAACC	6291
AD-1948266	guaucuUfuUfGfCfaacugaaacu	3330	PaGfuudTc(Agn)guugcaAfaAfgauacca	4811	UGGUAUCUUUUGCAACUGAAACC	6292
AD-1948267	uaucuuuuGfCfAfacugaaaccu	3331	PadGgudTudCaguudGcAfaaagauacc	4812	GGUAUCUUUUGCAACUGAAACCA	6293
AD-1948268	aucuuuugCfAfAfcugaaaccau	3332	PadTggdTudTcagudTgCfaaaagauac	4813	GUAUCUUUUGCAACUGAAACCAA	6294
AD-1948269	aucuuuUfgCfAfAfcugaaaccau	3333	PaUfggdTu(Tgn)caguugCfaAfaagauac	4814	GUAUCUUUUGCAACUGAAACCAA	6295
AD-1948270	ucuuuugcAfAfCfugaaaccaau	3334	PadTugdGudTucagdTuGfcaaaagaua	4815	UAUCUUUUGCAACUGAAACCAAU	6296
AD-1948271	ucuuuuGfcAfAfCfugaaaccaau	3335	PaUfugdGu(Tgn)ucaguuGfcAfaaagaua	4816	UAUCUUUUGCAACUGAAACCAAU	6297
AD-1948272	cuuuugcaAfCfUfgaaaccaauu	3336	PadAuudGgdTuucadGuUfgcaaaagau	4817	AUCUUUUGCAACUGAAACCAAUG	6298
AD-1948273	cuuuugCfaAfCfUfgaaaccaauu	3337	PaAfuudGg(Tgn)uucaguUfgCfaaaagau	4818	AUCUUUUGCAACUGAAACCAAUG	6299
AD-1948274	uuuugcaaCfUfGfaaaccaaugu	3338	PadCaudTgdGuuucdAgUfugcaaaaga	4819	UCUUUUGCAACUGAAACCAAUGG	6300
AD-1948275	uugcagauGfUfUfucugaguucu	3339	PadGaadCudCagaadAcAfucugcaaaa	4820	UUUUGCAGAUGUUUCUGAGUUCA	6301
AD-1948276	ugcagaugUfUfUfcugaguucau	3340	PadTgadAcdTcagadAaCfaucugcaaa	4821	UUUGCAGAUGUUUCUGAGUUCAA	6302

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948277	ugcagaUfgUfUfUfUfcugaguucau	3341	PaUfgadAc(Tgn)cagaaaCfaUfcugcaaa	4822	UUUGCAGAUGUUUCUGAGUUCAA	6303
AD-1948278	gcagauguUfUfCfugaguucaau	3342	PadTugdAadCucagdAaAfcaucugcaa	4823	UUGCAGAUGUUUCUGAGUUCAAG	6304
AD-1948279	cagauguuUfCfUfgaguucaagu	3343	PadCuudGadAcucadGaAfacaucugca	4824	UGCAGAUGUUUCUGAGUUCAAGC	6305
AD-1948280	cagaugUfuUfCfUfgaguucaagu	3344	PaCfuudGa(Agn)cucagaAfaCfaucugca	4825	UGCAGAUGUUUCUGAGUUCAAGC	6306
AD-1948281	agauguuuCfUfGfaguucaagcu	3345	PadGcudTgdAacucdAgAfaacaucugc	4826	GCAGAUGUUUCUGAGUUCAAGCA	6307
AD-1948282	agauguUfuCfUfGfaguucaagcu	3346	PaGfcudTg(Agn)acucagAfaAfcaucugc	4827	GCAGAUGUUUCUGAGUUCAAGCA	6308
AD-1948283	gauguuucUfGfAfguucaagcau	3347	PadTgcdTudGaacudCaGfaaacaucug	4828	CAGAUGUUUCUGAGUUCAAGCAC	6309
AD-1948284	auguuucuGfAfGfucaagcacu	3348	PadGugdCudTgaacdTcAfgaaacaucu	4829	AGAUGUUUCUGAGUUCAAGCACA	6310
AD-1948285	auguuuCfuGfAfGfuucaagcacu	3349	PaGfugdCu(Tgn)gaacucAfgAfaacaucu	4830	AGAUGUUUCUGAGUUCAAGCACA	6311
AD-1948286	uguuucugAfGfUfucaagcacau	3350	PadTgudGcdTugaadCuCfagaaacauc	4831	GAUGUUUCUGAGUUCAAGCACAU	6312
AD-1948287	uguuucUfgAfGfUfucaagcacau	3351	PaUfgudGc(Tgn)ugaacuCfaGfaaacauc	4832	GAUGUUUCUGAGUUCAAGCACAU	6313
AD-1948288	guuucugaGfUfUfcaagcacauu	3352	PadAugdTgdCuugadAcUfcagaaacau	4833	AUGUUUCUGAGUUCAAGCACAUA	6314
AD-1948289	uuucugagUfUfCfaagcacauau	3353	PadTaudGudGcuugdAaCfucagaaaca	4834	UGUUUCUGAGUUCAAGCACAUAU	6315
AD-1948290	auccugaaAfUfUfcaugguuucu	3354	PadGaadAcdCaugadAuUfucaggauau	4835	AUAUCCUGAAAUUCAUGGUUUCU	6316
AD-1948291	uccugaaaUfUfCfaugguuucuu	3355	PadAgadAadCcaugdAaUfuucaggaua	4836	UAUCCUGAAAUUCAUGGUUUCUU	6317
AD-1948292	ccugaaauUfCfAfugguuucuuu	3356	PadAagdAadAccaudGaAfuuucaggau	4837	AUCCUGAAAUUCAUGGUUUCUUA	6318
AD-1948293	cugaaauuCfAfUfgguuucuuau	3357	PadTaadGadAaccadTgAfauuucagga	4838	UCCUGAAAUUCAUGGUUUCUUAC	6319
AD-1948294	ugaaauucAfUfGfguuucuuacu	3358	PadGuadAgdAaaccdAuGfaauuucagg	4839	CCUGAAAUUCAUGGUUUCUUACA	6320
AD-1948295	ugaaauUfcAfUfGfguuucuuacu	3359	PaGfuadAg(Agn)aaccauGfaAfuuucagg	4840	CCUGAAAUUCAUGGUUUCUUACA	6321
AD-1948296	gaaauucaUfGfGfuuucuuacau	3360	PadTgudAadGaaacdCaUfgaauuucag	4841	CUGAAAUUCAUGGUUUCUUACAU	6322
AD-1948297	aaauucauGfGfUfucuuacauu	3361	PadAugdTadAgaaadCcAfugaauuuca	4842	UGAAAUUCAUGGUUUCUUACAUG	6323
AD-1948298	aauucaugGfUfUfucuuacaugu	3362	PadCaudGudAagaadAcCfaugaauuuc	4843	GAAAUUCAUGGUUUCUUACAUGC	6324
AD-1948299	auucauggUfUfUfcuuacaugcu	3363	PadGcadTgdTaagadAaCfcaugaauuu	4844	AAAUUCAUGGUUUCUUACAUGCG	6325
AD-1948300	auucauGfgUfUfUfcuuacaugcu	3364	PaGfcadTg(Tgn)aagaaaCfcAfugaauuu	4845	AAAUUCAUGGUUUCUUACAUGCG	6326

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948301	uucaugguUfUfCfuuacaugcgu	3365	PadCgcdAudGuaagdAaAfccaugaauu	4846	AAUUCAUGGUUUCUUACAUGCGA	6327
AD-1948302	ucaugguuUfCfUfuacaugcgau	3366	PadTcgdCadTguaadGaAfaccaugaau	4847	AUUCAUGGUUUCUUACAUGCGAA	6328
AD-1948303	ucauggUfuUfCfUfuacaugcgau	3367	PaUfcgdCa(Tgn)guaagaAfaCfcaugaau	4848	AUUCAUGGUUUCUUACAUGCGAA	6329
AD-1948304	caugguuuCfUfUfacaugcgaau	3368	PadTucdGcdAuguadAgAfaaccaugaa	4849	UUCAUGGUUUCUUACAUGCGAAA	6330
AD-1948305	caugguUfuCfUfUfacaugcgaau	3369	PaUfucdGc(Agn)uguaagAfaAfccaugaa	4850	UUCAUGGUUUCUUACAUGCGAAA	6331
AD-1948306	augguuucUfUfAfcaugcgaaau	3370	PadTuudCgdCaugudAaGfaaaccauga	4851	UCAUGGUUUCUUACAUGCGAAAG	6332
AD-1948307	ugguuucuUfAfCfaugcgaaagu	3371	PadCuudTcdGcaugdTaAfgaaaccaug	4852	CAUGGUUUCUUACAUGCGAAAGA	6333
AD-1948308	gguuucuuAfCfAfugcgaaagau	3372	PadTcudTudCgcaudGuAfagaaaccau	4853	AUGGUUUCUUACAUGCGAAAGAA	6334
AD-1948309	guuucuuaCfAfUfgcgaaagaau	3373	PadTucdTudTcgcadTgUfaagaaacca	4854	UGGUUUCUUACAUGCGAAAGAAC	6335
AD-1948310	guuucuUfaCfAfUfgcgaaagaau	3374	PaUfucdTu(Tgn)cgcaugUfaAfgaaacca	4855	UGGUUUCUUACAUGCGAAAGAAC	6336
AD-1948311	uuucuuacAfUfGfcgaaagaacu	3375	PadGuudCudTucgcdAuGfuaagaaacc	4856	GGUUUCUUACAUGCGAAAGAACA	6337
AD-1948312	uuucuuAfcAfUfGfcgaaagaacu	3376	PaGfuudCu(Tgn)ucgcauGfuAfagaaacc	4857	GGUUUCUUACAUGCGAAAGAACA	6338
AD-1948313	uucuuacaUfGfCfgaaagaacau	3377	PadTgudTcdTuucgdCaUfguaagaaac	4858	GUUUCUUACAUGCGAAAGAACAG	6339
AD-1948314	uucuuaCfaUfGfCfgaaagaacau	3378	PaUfgudTc(Tgn)uucgcaUfgUfaagaaac	4859	GUUUCUUACAUGCGAAAGAACAG	6340
AD-1948315	ucuuacauGfCfGfaaagaacagu	3379	PadCugdTudCuuucdGcAfuguaagaaa	4860	UUUCUUACAUGCGAAAGAACAGG	6341
AD-1948316	uacaugcgAfAfAfgaacagggau	3380	PadTccdCudGuucudTuCfgcauguaag	4861	CUUACAUGCGAAAGAACAGGGAA	6342
AD-1948317	acaugcgaAfAfGfaacagggaau	3381	PadTucdCcdTguucdTuUfcgcauguaa	4862	UUACAUGCGAAAGAACAGGGAAA	6343
AD-1948318	acaugcGfaAfAfGfaacagggaau	3382	PaUfucdCc(Tgn)guucuuUfcGfcauguaa	4863	UUACAUGCGAAAGAACAGGGAAA	6344
AD-1948319	caugcgaaAfGfAfacagggaaau	3383	PadTuudCcdCuguudCuUfucgcaugua	4864	UACAUGCGAAAGAACAGGGAAAG	6345
AD-1948320	augcgaaaGfAfAfcagggaaagu	3384	PadCuudTcdCcugudTcUfuucgcaugu	4865	ACAUGCGAAAGAACAGGGAAAGA	6346
AD-1948321	ugcgaaagAfAfCfagggaaagau	3385	PadTcudTudCccugdTuCfuuucgcaug	4866	CAUGCGAAAGAACAGGGAAAGAA	6347
AD-1948322	gcgaaagaAfCfAfggaaagaau	3386	PadTucdTudTcccudGuUfcuuucgcau	4867	AUGCGAAAGAACAGGGAAAGAAG	6348
AD-1948323	gcgaaaGfaAfCfAfgggaaagaau	3387	PaUfucdTu(Tgn)cccuguUfcUfuucgcau	4868	AUGCGAAAGAACAGGGAAAGAAG	6349
AD-1948324	gaaagaacAfGfGfgaaagaaguu	3388	PadAcudTcdTuuccdCuGfuucuuucgc	4869	GCGAAAGAACAGGGAAAGAAGUC	6350

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948325	gaaagaAfcAfGfGfgaaagaaguu	3389	PaAfcudTc(Tgn)uucccuGfuUfcuuucgc	4870	GCGAAAGAACAGGGAAAGAAGUC	6351
AD-1948326	aaagaacaGfGfGfaaagaagucu	3390	PadGacdTudCuuucdCcUfguucuuucg	4871	CGAAAGAACAGGGAAAGAAGUCU	6352
AD-1948327	aagaacagGfGfAfaagaagucuu	3391	PadAgadCudTcuuudCcCfuguucuuuc	4872	GAAAGAACAGGGAAAGAAGUCUU	6353
AD-1948328	aagaacAfgGfGfAfaagaagucuu	3392	PaAfgadCu(Tgn)cuuuccCfuGfuucuuuc	4873	GAAAGAACAGGGAAAGAAGUCUU	6354
AD-1948329	agaacaggGfAfAfagaagucuuu	3393	PadAagdAcdTucuudTcCfcuguucuuu	4874	AAAGAACAGGGAAAGAAGUCUUG	6355
AD-1948330	agaacaGfgGfAfAfagaagucuuu	3394	PaAfagdAc(Tgn)ucuuucCfcUfguucuuu	4875	AAAGAACAGGGAAAGAAGUCUUG	6356
AD-1948331	gaacagggAfAfAfgaagucuugu	3395	PadCaadGadCuucudTuCfccuguucuu	4876	AAGAACAGGGAAAGAAGUCUUGG	6357
AD-1948332	acagggaaAfGfAfagucuuggau	3396	PadTccdAadGacuudCuUfucccuguuc	4877	GAACAGGGAAAGAAGUCUUGGAA	6358
AD-1948333	cagggaaaGfAfAfgucuuggaau	3397	PadTucdCadAgacudTcUfuucccuguu	4878	AACAGGGAAAGAAGUCUUGGAAA	6359
AD-1948334	cagggaAfaGfAfAfgucuuggaau	3398	PaUfucdCa(Agn)gacuucUfuUfcccuguu	4879	AACAGGGAAAGAAGUCUUGGAAA	6360
AD-1948335	agggaaagAfAfGfucuuggaaau	3399	PadTuudCcdAagacdTuCfuuucccugu	4880	ACAGGGAAAGAAGUCUUGGAAAA	6361
AD-1948336	agggaaAfgAfAfGfucuuggaaau	3400	PaUfuudCc(Agn)agacuuCfuUfucccugu	4881	ACAGGGAAAGAAGUCUUGGAAAA	6362
AD-1948337	gggaaagaAfGfUfcuuggaaaau	3401	PadTuudTcdCaagadCuUfcuuucccug	4882	CAGGGAAAGAAGUCUUGGAAAAA	6363
AD-1948338	ggaaagaaGfUfCfuuggaaaaau	3402	PadTuudTudCcaagdAcUfucuuucccu	4883	AGGGAAAGAAGUCUUGGAAAAAA	6364
AD-1948339	gaaagaagUfCfUfuggaaaaaau	3403	PadTuudTudTccaadGaCfuucuuuccc	4884	GGGAAAGAAGUCUUGGAAAAAAA	6365
AD-1948340	gaaagaAfgUfCfUfuggaaaaaau	3404	PaUfuudTu(Tgn)ccaagaCfuUfcuuuccc	4885	GGGAAAGAAGUCUUGGAAAAAAA	6366
AD-1948341	aaagaaguCfUfUfggaaaaaaau	3405	PadTuudTudTuccadAgAfcuucuuucc	4886	GGAAAGAAGUCUUGGAAAAAAAU	6367
AD-1948342	aaagaaGfuCfUfUfggaaaaaaau	3406	PaUfuudTu(Tgn)uccaagAfcUfucuuucc	4887	GGAAAGAAGUCUUGGAAAAAAAU	6368
AD-1948343	aagaagucUfUfGfgaaaaaauu	3407	PadAuudTudTuuccdAaGfacuucuuuc	4888	GAAAGAAGUCUUGGAAAAAAAUU	6369
AD-1948344	aagaagUfcUfUfGfgaaaaaauu	3408	PaAfuudTu(Tgn)uuccaaGfaCfuucuuuc	4889	GAAAGAAGUCUUGGAAAAAAAUU	6370
AD-1948345	aagucuugGfAfAfaaaauuuau	3409	PadTaadAudTuuuudTcCfaagacuucu	4890	AGAAGUCUUGGAAAAAAUUUAC	6371
AD-1948346	agucuuggAfAfAfaaaauuuacu	3410	PadGuadAadTuuuudTuCfcaagacuuc	4891	GAAGUCUUGGAAAAAAUUUACU	6372
AD-1948347	acuuuuuuCfUfAfagaagaucuu	3411	PadAgadTcdTucuudAgAfaaaaaguaa	4892	UUACUUUUUUCUAAGAAGAUCUG	6373
AD-1948348	acuuuuUfuCfUfAfagaagaucuu	3412	PaAfgadTc(Tgn)ucuuagAfaAfaaaguaa	4893	UUACUUUUUUCUAAGAAGAUCUG	6374

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948349	cuuuuuucUfAfAfgaagaucugu	3413	PadCagdAudCuucudTaGfaaaaaagua	4894	UACUUUUUUCUAAGAAGAUCUGG	6375
AD-1948350	uuuuuucuAfAfGfaagaucuggu	3414	PadCcadGadTcuucdTuAfgaaaaaagu	4895	ACUUUUUUCUAAGAAGAUCUGGU	6376
AD-1948351	uuuuucuaAfGfAfagaucugguu	3415	PadAccdAgdAucuudCuUfagaaaaaag	4896	CUUUUUUCUAAGAAGAUCUGGUU	6377
AD-1948352	uuuuucUfaAfGfAfagaucugguu	3416	PaAfccdAg(Agn)ucuucuUfaGfaaaaaag	4897	CUUUUUUCUAAGAAGAUCUGGUU	6378
AD-1948353	uuuucuaaGfAfAfgaucugguuu	3417	PadAacdCadGaucudTcUfuagaaaaaa	4898	UUUUUUCUAAGAAGAUCUGGUUU	6379
AD-1948354	uuucuaagAfAfGfaucugguuuu	3418	PadAaadCcdAgaucdTuCfuuagaaaaa	4899	UUUUUCUAAGAAGAUCUGGUUUA	6380
AD-1948355	uuucuaAfgAfAfGfaucugguuuu	3419	PaAfaadCc(Agn)gaucuuCfuUfagaaaaa	4900	UUUUUCUAAGAAGAUCUGGUUUA	6381
AD-1948356	uucuaagaAfGfAfucugguuuau	3420	PadTaadAcdCagaudCuUfcuuagaaaa	4901	UUUUCUAAGAAGAUCUGGUUUAU	6382
AD-1948357	ucuaagaaGfAfUfcugguuuauu	3421	PadAuadAadCcagadTcUfucuuagaaa	4902	UUUCUAAGAAGAUCUGGUUUAUA	6383
AD-1948358	cuaagaagAfUfCfugguuuauau	3422	PadTaudAadAccagdAuCfuucuuagaa	4903	UUCUAAGAAGAUCUGGUUUAUAU	6384
AD-1948359	uaagaagaUfCfUfgguuuauauu	3423	PadAuadTadAaccadGaUfcuucuuaga	4904	UCUAAGAAGAUCUGGUUUAUAUU	6385
AD-1948360	aagaagauCfUfGfguuuauauuu	3424	PadAaudAudAaaccdAgAfucuucuuag	4905	CUAAGAAGAUCUGGUUUAUAUUU	6386
AD-1948361	aagaucugGfUfUfuauauuuuuu	3425	PadAaadAadTauaadAcCfagaucuucu	4906	AGAAGAUCUGGUUUAUAUUUUUC	6387
AD-1948362	agaucuggUfUfUfauauuuuucu	3426	PadGaadAadAuauadAaCfcagaucuuc	4907	GAAGAUCUGGUUUAUAUUUUUCU	6388
AD-1948363	aucugguuUfAfUfauuuuucuau	3427	PadTagdAadAaauadTaAfaccagaucu	4908	AGAUCUGGUUUAUAUUUUUCUAC	6389
AD-1948364	ucugguuuAfUfAfuuuuucuacu	3428	PadGuadGadAaaaudAuAfaaccagauc	4909	GAUCUGGUUUAUAUUUUUCUACU	6390
AD-1948365	uuuauauuUfUfUfcuacuaaagu	3429	PadCuudTadGuagadAaAfauauaaacc	4910	GGUUUAUAUUUUUCUACUAAAGG	6391
AD-1948366	ucaaaggaAfCfCfggcgauuuu	3430	PadAaadTgdCcgcgdGuUfccuuugaug	4911	CAUCAAAGGAACCGCGGCAUUUG	6392
AD-1948367	aaggaaccGfCfGfgcauuugcau	3431	PadTgcdAadAugccdGcGfguuccuuug	4912	CAAAGGAACCGCGGCAUUUGCAG	6393
AD-1948368	aggaaccgCfGfGfcauuugcagu	3432	PadCugdCadAaugcdCgCfgguuccuuu	4913	AAAGGAACCGCGGCAUUUGCAGU	6394
AD-1948369	gaaccgcgGfCfAfuuugcaguuu	3433	PadAacdTgdCaaaudGcCfgcgguuccu	4914	AGGAACCGCGGCAUUUGCAGUUU	6395
AD-1948370	aaccgcggCfAfUfuugcaguuuu	3434	PadAaadCudGcaaadTgCfcgcgguucc	4915	GGAACCGCGGCAUUUGCAGUUUU	6396
AD-1948371	ccgcggcaUfUfUfgcaguuuuuu	3435	PadAaadAadCugcadAaUfgccgcgguu	4916	AACCGCGGCAUUUGCAGUUUUUC	6397
AD-1948372	gcggcauuUfGfCfaguuuuucau	3436	PadTgadAadAacugdCaAfaugccgcgg	4917	CCGCGGCAUUUGCAGUUUUUCAG	6398

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948373	cggcauuuGfCfAfguuuuucagu	3437	PadCugdAadAaacudGcAfaaugccgcg	4918	CGCGGCAUUUGCAGUUUUUCAGC	6399
AD-1948374	ggcauuugCfAfGfuuuuucagcu	3438	PadGcudGadAaaacdTgCfaaaugccgc	4919	GCGGCAUUUGCAGUUUUUCAGCG	6400
AD-1948375	gcauuugcAfGfUfuuuucagcgu	3439	PadCgcdTgdAaaaadCuGfcaaaugccg	4920	CGGCAUUUGCAGUUUUUCAGCGA	6401
AD-1948376	gcauuuGfcAfGfUfuuuucagcgu	3440	PaCfgcdTg(Agn)aaaacuGfcAfaaugccg	4921	CGGCAUUUGCAGUUUUUCAGCGA	6402
AD-1948377	cauuugcaGfUfUfuuucagcgau	3441	PadTcgdCudGaaaadAcUfgcaaaugcc	4922	GGCAUUUGCAGUUUUUCAGCGAA	6403
AD-1948378	auuugcagUfUfUfuucagcgaau	3442	PadTucdGcdTgaaadAaCfugcaaaugc	4923	GCAUUUGCAGUUUUUCAGCGAAU	6404
AD-1948379	auuugcAfgUfUfUfuucagcgaau	3443	PaUfucdGc(Tgn)gaaaaCfuGfcaaaugc	4924	GCAUUUGCAGUUUUUCAGCGAAU	6405
AD-1948380	uuugcaguUfUfUfucagcgaauu	3444	PadAuudCgdCugaadAaAfcugcaaaug	4925	CAUUUGCAGUUUUUCAGCGAAUU	6406
AD-1948381	uugcaguuUfUfUfcagcgaauuu	3445	PadAaudTcdGcugadAaAfacugcaaau	4926	AUUUGCAGUUUUUCAGCGAAUUU	6407
AD-1948382	ugcaguuuUfUfCfagcgaauuuu	3446	PadAaadTudCgcugdAaAfaacugcaaa	4927	UUUGCAGUUUUUCAGCGAAUUUG	6408
AD-1948383	gcaguuuuUfCfAfgcgaauuugu	3447	PadCaadAudTcgcudGaAfaaacugcaa	4928	UUGCAGUUUUUCAGCGAAUUUGG	6409
AD-1948384	caguuuuuCfAfGfcgaauuuggu	3448	PadCcadAadTucgcdTgAfaaaacugca	4929	UGCAGUUUUUCAGCGAAUUUGGC	6410
AD-1948385	aguuuuucAfGfCfgaauuuggcu	3449	PadGccdAadAuucgdCuGfaaaaacugc	4930	GCAGUUUUUCAGCGAAUUUGGCA	6411
AD-1948386	guuuuucaGfCfGfaauuuggcau	3450	PadTgcdCadAauucdGcUfgaaaaacug	4931	CAGUUUUUCAGCGAAUUUGGCAA	6412
AD-1948387	uuuuucagCfGfAfauuuggcaau	3451	PadTugdCcdAaauudCgCfugaaaaacu	4932	AGUUUUUCAGCGAAUUUGGCAAU	6413
AD-1948388	uuuuucAfgCfGfAfauuuggcaau	3452	PaUfugdCc(Agn)aauucgCfuGfaaaaacu	4933	AGUUUUUCAGCGAAUUUGGCAAU	6414
AD-1948389	uuuucagcGfAfAfuuuggcaauu	3453	PadAuudGcdCaaaudTcGfcugaaaaac	4934	GUUUUUCAGCGAAUUUGGCAAUA	6415
AD-1948390	uuucagcgAfAfUfuuggcaauau	3454	PadTaudTgdCcaaadTuCfgcugaaaaa	4935	UUUUUCAGCGAAUUUGGCAAUAG	6416
AD-1948391	uucagcgaAfUfUfuggcaauagu	3455	PadCuadTudGccaadAuUfcgcugaaaa	4936	UUUUCAGCGAAUUUGGCAAUAGU	6417
AD-1948392	ucagcgaaUfUfUfggcaauaguu	3456	PadAcudAudTgccadAaUfucgcugaaa	4937	UUUCAGCGAAUUUGGCAAUAGUG	6418
AD-1948393	cagcgaauUfUfGfgcaauagugu	3457	PadCacdTadTugccdAaAfuucgcugaa	4938	UUCAGCGAAUUUGGCAAUAGUGA	6419
AD-1948394	agcgaauuUfGfGfcaauagugau	3458	PadTcadCudAuugcdCaAfauucgcuga	4939	UCAGCGAAUUUGGCAAUAGUGAU	6420
AD-1948395	gcgaauuuGfGfCfaauagugauu	3459	PadAucdAcdTauugdCcAfaauucgcug	4940	CAGCGAAUUUGGCAAUAGUGAUA	6421
AD-1948396	gcgaauUfuGfGfCfaauagugauu	3460	PaAfucdAc(Tgn)auugccAfaAfuucgcug	4941	CAGCGAAUUUGGCAAUAGUGAUA	6422

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948397	cgaauuugGfCfAfauagugauau	3461	PadTaudCadCuauudGcCfaaauucgcu	4942	AGCGAAUUUGGCAAUAGUGAUAU	6423
AD-1948398	gaauuuggCfAfAfuagugauauu	3462	PadAuadTcdAcuaudTgCfcaaauucgc	4943	GCGAAUUUGGCAAUAGUGAUAUU	6424
AD-1948399	gaauuuGfgCfAfAfuagugauauu	3463	PaAfuadTc(Agn)cuauugCfcAfaauucgc	4944	GCGAAUUUGGCAAUAGUGAUAUU	6425
AD-1948400	aauuuggcAfAfUfagugauauuu	3464	PadAaudAudCacuadTuGfccaaauucg	4945	CGAAUUUGGCAAUAGUGAUAUUU	6426
AD-1948401	auuuggcaAfUfAfgugauauuuu	3465	PadAaadTadTcacudAuUfgccaaauuc	4946	GAAUUUGGCAAUAGUGAUAUUUA	6427
AD-1948402	auuuggCfaAfUfAfgugauauuuu	3466	PaAfaadTa(Tgn)cacuauUfgCfcaaauuc	4947	GAAUUUGGCAAUAGUGAUAUUUA	6428
AD-1948403	uuggcaauAfGfUfgauauuuauu	3467	PadAuadAadTaucadCuAfuugccaaau	4948	AUUUGGCAAUAGUGAUAUUUAUG	6429
AD-1948404	uggcaauaGfUfGfauauuuaugu	3468	PadCaudAadAuaucdAcUfauugccaaa	4949	UUUGGCAAUAGUGAUAUUUAUGU	6430
AD-1948405	ggcaauagUfGfAfuauuuauguu	3469	PadAcadTadAauaudCaCfuauugccaa	4950	UUGGCAAUAGUGAUAUUUAUGUG	6431
AD-1948406	gcaauaguGfAfUfauuuaugugu	3470	PadCacdAudAaauadTcAfcuauugcca	4951	UGGCAAUAGUGAUAUUUAUGUGU	6432
AD-1948407	caauagugAfUfAfuuauguguu	3471	PadAcadCadTaaaudAuCfacuauugcc	4952	GGCAAUAGUGAUAUUUAUGUGUC	6433
AD-1948408	aauagugaUfAfUfuuaugugucu	3472	PadGacdAcdAuaaadTaUfcacuauugc	4953	GCAAUAGUGAUAUUUAUGUGUCA	6434
AD-1948409	aauaguGfaUfAfUfuuaugugucu	3473	PaGfacdAc(Agn)uaaauaUfcAfcuauugc	4954	GCAAUAGUGAUAUUUAUGUGUCA	6435
AD-1948410	aacauggaGfCfAfccgacuaacu	3474	PadGuudAgdTcggudGcUfccauguuuu	4955	AAAACAUGGAGCACCGACUAACU	6436
AD-1948411	aacaugGfaGfCfAfccgacuaacu	3475	PaGfuudAg(Tgn)cgggcUfcCfauguuuu	4956	AAAACAUGGAGCACCGACUAACU	6437
AD-1948412	acauggagCfAfCfcgacuaacuu	3476	PadAgudTadGucggdTgCfuccauguuu	4957	AAACAUGGAGCACCGACUAACUA	6438
AD-1948413	cauggagcAfCfCfgacuaacuau	3477	PadTagdTudAgucgdGuGfcuccauguu	4958	AACAUGGAGCACCGACUAACUAU	6439
AD-1948414	cauggaGfcAfCfCfgacuaacuau	3478	PaUfagdTu(Agn)gucgguGfcUfccauguu	4959	AACAUGGAGCACCGACUAACUAU	6440
AD-1948415	auggagcaCfCfGfacuaacuau	3479	PadAuadGudTagucdGgUfgcuccaugu	4960	ACAUGGAGCACCGACUAACUAUG	6441
AD-1948416	auggagCfaCfCfGfacuaacuauu	3480	PaAfuadGu(Tgn)agucggUfgCfuccaugu	4961	ACAUGGAGCACCGACUAACUAUG	6442
AD-1948417	uggagcacCfGfAfcuaacuaugu	3481	PadCaudAgdTuagudCgGfugcuccaug	4962	CAUGGAGCACCGACUAACUAUGG	6443
AD-1948418	ggagcaccGfAfCfuaacuauggu	3482	PadCcadTadGuuagdTcGfgugcuccau	4963	AUGGAGCACCGACUAACUAUGGA	6444
AD-1948419	gagcaccgAfCfUfaacuauggau	3483	PadTccdAudAguuadGuCfggugcucca	4964	UGGAGCACCGACUAACUAUGGAU	6445
AD-1948420	agcaccgaCfUfAfacuauggauu	3484	PadAucdCadTaguudAgUfcggugcucc	4965	GGAGCACCGACUAACUAUGGAUU	6446

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948421	gcaccgacUfAfAfcuauggauuu	3485	PadAaudCcdAuagudTaGfucggugcuc	4966	GAGCACCGACUAACUAUGGAUUC	6447
AD-1948422	gcaccgAfcUfAfAfcuauggauuu	3486	PaAfaudCc(Agn)uaguuaGfuCfggugcuc	4967	GAGCACCGACUAACUAUGGAUUC	6448
AD-1948423	caccgacuAfAfCfuauggauucu	3487	PadGaadTcdCauagdTuAfgucggugcu	4968	AGCACCGACUAACUAUGGAUUCU	6449
AD-1948424	accgacuaAfCfUfauggauucuu	3488	PadAgadAudCcauadGuUfagucggugc	4969	GCACCGACUAACUAUGGAUUCUG	6450
AD-1948425	ccgacuaaCfUfAfuggauucugu	3489	PadCagdAadTccaudAgUfuagucggug	4970	CACCGACUAACUAUGGAUUCUGC	6451
AD-1948426	cgacuaacUfAfUfggauucugcu	3490	PadGcadGadAuccadTaGfuuagucggu	4971	ACCGACUAACUAUGGAUUCUGCU	6452
AD-1948427	cgacuaAfcUfAfUfggauucugcu	3491	PaGfcadGa(Agn)uccauaGfuUfagucggu	4972	ACCGACUAACUAUGGAUUCUGCU	6453
AD-1948428	gacuaacuAfUfGfgauucugcuu	3492	PadAgcdAgdAauccdAuAfguuagucgg	4973	CCGACUAACUAUGGAUUCUGCUU	6454
AD-1948429	gacuaaCfuAfUfGfgauucugcuu	3493	PaAfgcdAg(Agn)auccauAfgUfuagucgg	4974	CCGACUAACUAUGGAUUCUGCUU	6455
AD-1948430	acuaacuaUfGfGfaucugcuuu	3494	PadAagdCadGaaucdCaUfaguuagucg	4975	CGACUAACUAUGGAUUCUGCUUU	6456
AD-1948431	cuaacuauGfGfAfucugcuuuu	3495	PadAaadGcdAgaaudCcAfuaguuaguc	4976	GACUAACUAUGGAUUCUGCUUUA	6457
AD-1948432	cuaacuAfuGfGfAfuucugcuuuu	3496	PaAfaadGc(Agn)gaauccAfuAfguuaguc	4977	GACUAACUAUGGAUUCUGCUUUA	6458
AD-1948433	uaacuaugGfAfUfucugcuuuau	3497	PadTaadAgdCagaadTcCfauaguuagu	4978	ACUAACUAUGGAUUCUGCUUUAA	6459
AD-1948434	aacuauggAfUfUfcugcuuuaau	3498	PadTuadAadGcagadAuCfcauaguuag	4979	CUAACUAUGGAUUCUGCUUUAAG	6460
AD-1948435	acuauggaUfUfCfugcuuuaagu	3499	PadCuudAadAgcagdAaUfccauaguua	4980	UAACUAUGGAUUCUGCUUUAAGC	6461
AD-1948436	cuauggauUfCfUfgcuuuaagcu	3500	PadGcudTadAagcadGaAfuccauaguu	4981	AACUAUGGAUUCUGCUUUAAGCC	6462
AD-1948437	uauggauuCfUfGfcuuuaagccu	3501	PadGgcdTudAaagcdAgAfauccauagu	4982	ACUAUGGAUUCUGCUUUAAGCCU	6463
AD-1948438	auggauucUfGfCfuuuaagccuu	3502	PadAggdCudTaaagdCaGfaauccauag	4983	CUAUGGAUUCUGCUUUAAGCCUA	6464
AD-1948439	auggauUfcUfGfCfuuuaagccuu	3503	PaAfggdCu(Tgn)aaagcaGfaAfuccauag	4984	CUAUGGAUUCUGCUUUAAGCCUA	6465
AD-1948440	uggauucuGfCfUfuuaagccuau	3504	PadTagdGcdTuaaadGcAfgaauccaua	4985	UAUGGAUUCUGCUUUAAGCCUAA	6466
AD-1948441	uggauuCfuGfCfUfuuaagccuau	3505	PaUfagdGc(Tgn)uaaagcAfgAfauccaua	4986	UAUGGAUUCUGCUUUAAGCCUAA	6467
AD-1948442	ggauucugCfUfUfuaagccuaau	3506	PadTuadGgdCuuaadAgCfagaauccau	4987	AUGGAUUCUGCUUUAAGCCUAAC	6468
AD-1948443	gauucugcUfUfUfaagccuaacu	3507	PadGuudAgdGcuuadAaGfcagaaucca	4988	UGGAUUCUGCUUUAAGCCUAACA	6469
AD-1948444	auucugcuUfUfAfagccuaacau	3508	PadTgudTadGgcuudAaAfgcagaaucc	4989	GGAUUCUGCUUUAAGCCUAACAA	6470

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948445	uucugcuuUfAfAfgccuaacaau	3509	PadTugdTudAggcudTaAfagcagaauc	4990	GAUUCUGCUUUAAGCCUAACAAA	6471
AD-1948446	uucugcUfuUfAfAfgccuaacaau	3510	PaUfugdTu(Agn)ggcuuaAfaGfcagaauc	4991	GAUUCUGCUUUAAGCCUAACAAA	6472
AD-1948447	ucugcuuuAfAfGfccuaacaaau	3511	PadTuudGudTaggcdTuAfaagcagaau	4992	AUUCUGCUUUAAGCCUAACAAAG	6473
AD-1948448	ucugcuUfuAfAfGfccuaacaaau	3512	PaUfuudGu(Tgn)aggcuuAfaAfgcagaau	4993	AUUCUGCUUUAAGCCUAACAAAG	6474
AD-1948449	cugcuuuaAfGfCfcuaacaaagu	3513	PadCuudTgdTuaggdCuUfaaagcagaa	4994	UUCUGCUUUAAGCCUAACAAAGC	6475
AD-1948450	cugcuuUfaAfGfCfcuaacaaagu	3514	PaCfuudTg(Tgn)uaggcuUfaAfagcagaa	4995	UUCUGCUUUAAGCCUAACAAAGC	6476
AD-1948451	ugcuuuaaGfCfCfuaacaaagcu	3515	PadGcudTudGuuagdGcUfuaaagcaga	4996	UCUGCUUUAAGCCUAACAAAGCG	6477
AD-1948452	cgagaccuGfAfAfaaugcucugu	3516	PadCagdAgdCauuudTcAfggucucggg	4997	CCCGAGACCUGAAAAUGCUCUGU	6478
AD-1948453	gagaccugAfAfAfaugcucuguu	3517	PadAcadGadGcauudTuCfaggucucgg	4998	CCGAGACCUGAAAAUGCUCUGUG	6479
AD-1948454	agaccugaAfAfAfugcucugugu	3518	PadCacdAgdAgcaudTuUfcaggucucg	4999	CGAGACCUGAAAAUGCUCUGUGC	6480
AD-1948455	agaccuGfaAfAfAfugcucugugu	3519	PaCfacdAg(Agn)gcauuuUfcAfggucucg	5000	CGAGACCUGAAAAUGCUCUGUGC	6481
AD-1948456	gaccugaaAfAfUfgcucugugcu	3520	PadGcadCadGagcadTuUfucaggucuc	5001	GAGACCUGAAAAUGCUCUGUGCA	6482
AD-1948457	accugaaaAfUfGfcucugugcau	3521	PadTgcdAcdAgagcdAuUfuucaggucu	5002	AGACCUGAAAAUGCUCUGUGCAG	6483
AD-1948458	accugaAfaAfUfGfcucugugcau	3522	PaUfgcdAc(Agn)gagcauUfuUfcaggucu	5003	AGACCUGAAAAUGCUCUGUGCAG	6484
AD-1948459	ccugaaaaUfGfCfucugugcagu	3523	PadCugdCadCagagdCaUfuuucagguc	5004	GACCUGAAAAUGCUCUGUGCAGA	6485
AD-1948460	cugaaaauGfCfUfcugugcagau	3524	PadTcudGcdAcagadGcAfuuuucaggu	5005	ACCUGAAAAUGCUCUGUGCAGAA	6486
AD-1948461	cugaaaAfuGfCfUfcugugcagau	3525	PaUfcudGc(Agn)cagagcAfuUfuucaggu	5006	ACCUGAAAAUGCUCUGUGCAGAA	6487
AD-1948462	ugaaaaugCfUfCfugugcagaau	3526	PadTucdTgdCacagdAgCfauuuucagg	5007	CCUGAAAAUGCUCUGUGCAGAAG	6488
AD-1948463	gaaaaugcUfCfUfgugcagaagu	3527	PadCuudCudGcacadGaGfcauuuucag	5008	CUGAAAAUGCUCUGUGCAGAAGA	6489
AD-1948464	aaaaugcuCfUfGfugcagaagau	3528	PadTcudTcdTgcacdAgAfgcauuuuca	5009	UGAAAAUGCUCUGUGCAGAAGAA	6490
AD-1948465	aaaaugCfuCfUfGfugcagaagau	3529	PaUfcudTc(Tgn)gcacagAfgCfauuuuca	5010	UGAAAAUGCUCUGUGCAGAAGAA	6491
AD-1948466	aaaugcucUfGfUfgcagaagaau	3530	PadTucdTudCugcadCaGfagcauuuuc	5011	GAAAAUGCUCUGUGCAGAAGAAG	6492
AD-1948467	aaugcucuGfUfGfcagaagaagu	3531	PadCuudCudTcugcdAcAfgagcauuuu	5012	AAAAUGCUCUGUGCAGAAGAAGA	6493
AD-1948468	augcucugUfGfCfagaagaagau	3532	PadTcudTcdTucugdCaCfagagcauuu	5013	AAAUGCUCUGUGCAGAAGAAGAG	6494

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948469	augcucUfgUfGfCfagaagaagau	3533	PaUfcudTc(Tgn)ucugcaCfaGfagcauuu	5014	AAAUGCUCUGUGCAGAAGAAGAG	6495
AD-1948470	cucugugcAfGfAfagaagagcau	3534	PadTgcdTcdTucuudCuGfcacagagca	5015	UGCUCUGUGCAGAAGAAGCAG	6496
AD-1948471	cucuguGfcAfGfAfagaagagcau	3535	PaUfgcdTc(Tgn)ucuucuGfcAfcagagca	5016	UGCUCUGUGCAGAAGAAGCAG	6497
AD-1948472	ucugugcaGfAfAfgaagagcagu	3536	PadCugdCudCuucudTcUfgcacagagc	5017	GCUCUGUGCAGAAGAAGAGCAGA	6498
AD-1948473	ugugcagaAfGfAfagagcagagu	3537	PadCucdTgdCucuudCuUfcugcacaga	5018	UCUGUGCAGAAGAAGAGCAGAGU	6499
AD-1948474	gugcagaaGfAfAfgagcagaguu	3538	PadAcudCudGcucudTcUfucugcacag	5019	CUGUGCAGAAGAAGAGCAGAGUA	6500
AD-1948475	ugcagaagAfAfGfagcagaguau	3539	PadTacdTcdTgcucdTuCfuucugcaca	5020	UGUGCAGAAGAAGAGCAGAGUAG	6501
AD-1948476	ugcagaAfgAfAfGfagcagaguau	3540	PaUfacdTc(Tgn)gcucuuCfuUfcugcaca	5021	UGUGCAGAAGAAGAGCAGAGUAG	6502
AD-1948477	gcagaagaAfGfAfgcagaguagu	3541	PadCuadCudCugcudCuUfcuucugcac	5022	GUGCAGAAGAAGAGCAGAGUAGG	6503
AD-1948478	cagaagaaGfAfGfcagaguaggu	3542	PadCcudAcdTcugcdTcUfucuucugca	5023	UGCAGAAGAAGAGCAGAGUAGGA	6504
AD-1948479	agaagaagAfGfCfagaguaggau	3543	PadTccdTadCucugdCuCfuucuucugc	5024	GCAGAAGAAGAGCAGAGUAGGAC	6505
AD-1948480	gaagaagaGfCfAfgaguaggacu	3544	PadGucdCudAcucudGcUfcuucuucug	5025	CAGAAGAAGAGCAGAGUAGGACG	6506
AD-1948481	gaagaaGfaGfCfAfgaguaggacu	3545	PaGfucdCu(Agn)cucugcUfcUfucuucug	5026	CAGAAGAAGAGCAGAGUAGGACG	6507
AD-1948482	agagcagaGfUfAfggacgugcuu	3546	PadAgcdAcdGuccudAcUfcugcucuuc	5027	GAAGAGCAGAGUAGGACGUGCUG	6508
AD-1948483	agaguaggAfCfGfugcugggugu	3547	PadCacdCcdAgcacdGuCfcuacucugc	5028	GCAGAGUAGGACGUGCUGGGUGA	6509
AD-1948484	gaguaggaCfGfUfgcugggugau	3548	PadTcadCcdCagcadCgUfccuacucug	5029	CAGAGUAGGACGUGCUGGGUGAC	6510
AD-1948485	cgugcuggGfUfGfaccgcgauuu	3549	PadAaudCgdCggucdAcCfcagcacguc	5030	GACGUGCUGGGUGACCGCGAUUA	6511
AD-1948486	gugcugggUfGfAfccgcgauuau	3550	PadTaadTcdGcggudCaCfccagcacgu	5031	ACGUGCUGGGUGACCGCGAUUAG	6512
AD-1948487	ugcuggguGfAfCfcgcgauuagu	3551	PadCuadAudCgcggdTcAfcccagcacg	5032	CGUGCUGGGUGACCGCGAUUAGA	6513
AD-1948488	cugggugaCfCfGfcgauuagauu	3552	PadAucdTadAucgcdGgUfcacccagca	5033	UGCUGGGUGACCGCGAUUAGAUU	6514
AD-1948489	ugggugacCfGfCfgauuagauuu	3553	PadAaudCudAaucgdCgGfucacccagc	5034	GCUGGGUGACCGCGAUUAGAUUG	6515
AD-1948490	gggugaccGfCfGfauuagauugu	3554	PadCaadTcdTaaucdGcGfgucacccag	5035	CUGGGUGACCGCGAUUAGAUUGC	6516
AD-1948491	ggugaCfcGfCfGfauuagauugu	3555	PaCfaadTc(Tgn)aaucgcGfgUfcacccag	5036	CUGGGUGACCGCGAUUAGAUUGC	6517
AD-1948492	ggugaccgCfGfAfuuagauugcu	3556	PadGcadAudCuaaudCgCfggucaccca	5037	UGGGUGACCGCGAUUAGAUUGCU	6518

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948493	gugaccgcGfAfUfu agauugcuu	3557	PadAgcdAadTcuaadTc Gfcggucaccc	5038	GGGUGACCGCGAU UAGAUUGCUU	6519
AD-1948494	ugaccgcgAfUfUfa gauugcuuu	3558	PadAagdCadAucuadA uCfgcggucacc	5039	GGUGACCGCGAUU AGAUUGCUUA	6520
AD-1948495	gaccgcgaUfUfAfg auugcuuau	3559	PadTaadGcdAaucudAa Ufcgcggucac	5040	GUGACCGCGAUUA GAUUGCUUAA	6521
AD-1948496	gaccgcGfaUfUfAf gauugcuuau	3560	PaUfaadGc(Agn)aucua aUfcGfcggucac	5041	GUGACCGCGAUUA GAUUGCUUAA	6522
AD-1948497	accgcgauUfAfGfa uugcuuaau	3561	PadTuadAgdCaaucdTa Afucgcgguca	5042	UGACCGCGAUUAG AUUGCUUAAG	6523
AD-1948498	ccgcgauuAfGfAfu ugcuuaagu	3562	PadCuudAadGcaaudC uAfaucgcgguc	5043	GACCGCGAUUAGA UUGCUUAAGU	6524
AD-1948499	cgcgauuaGfAfUfu gcuuaaguu	3563	PadAcudTadAgcaadTc Ufaaucgcggu	5044	ACCGCGAUUAGAU UGCUUAAGUA	6525
AD-1948500	gcgauuagAfUfUfg cuuaaguau	3564	PadTacdTudAagcadAu Cfuaaucgcgg	5045	CCGCGAUUAGAUU GCUUAAGUAU	6526
AD-1948501	cgauuagaUfUfGfc uuaaguauu	3565	PadAuadCudTaagcdAa Ufcuaaucgcg	5046	CGCGAUUAGAUUG CUUAAGUAUG	6527
AD-1948502	gauuagauUfGfCfu uaaguaugu	3566	PadCaudAcdTuaagdCa Afucuaaucgc	5047	GCGAUUAGAUUGC UUAAGUAUGG	6528
AD-1948503	auuagauuGfCfUfu aaguauggu	3567	PadCcadTadCuuaadGc Afaucuaaucg	5048	CGAUUAGAUUGCU UAAGUAUGGC	6529
AD-1948504	uuagauugCfUfUfa aguauggcu	3568	PadGccdAudAcuuadA gCfaaucuaauc	5049	GAUUAGAUUGCUU AAGUAUGGCA	6530
AD-1948505	uagauugcUfUfAfa guauggcau	3569	PadTgcdCadTacuudAa Gfcaaucuaau	5050	AUUAGAUUGCUUA AGUAUGGCAU	6531
AD-1948506	uagauuGfcUfUfAf aguauggcau	3570	PaUfgcdCa(Tgn)acuua aGfcAfaucuaau	5051	AUUAGAUUGCUUA AGUAUGGCAU	6532
AD-1948507	agauugcuUfAfAfg uauggcauu	3571	PadAugdCcdAuacudT aAfgcaaucuaa	5052	UUAGAUUGCUUAA GUAUGGCAUG	6533
AD-1948508	agauugCfuUfAfAf guauggcauu	3572	PaAfugdCc(Agn)uacuu aAfgCfaaucuaa	5053	UUAGAUUGCUUAA GUAUGGCAUG	6534
AD-1948509	gauugcuuAfAfGfu auggcaugu	3573	PadCaudGcdCauacdTu Afagcaaucua	5054	UAGAUUGCUUAAG UAUGGCAUGC	6535
AD-1948510	auugcuuaAfGfUfa uggcaugcu	3574	PadGcadTgdCcauadCu Ufaagcaaucu	5055	AGAUUGCUUAAGU AUGGCAUGCA	6536
AD-1948511	uugcuuaaGfUfAfu ggcaugcau	3575	PadTgcdAudGccaudA cUfuaagcaauc	5056	GAUUGCUUAAGUA UGGCAUGCAG	6537
AD-1948512	ugcuuaagUfAfUfg gcaugcagu	3576	PadCugdCadTgccadTa Cfuuaagcaau	5057	AUUGCUUAAGUAU GGCAUGCAGC	6538
AD-1948513	ugcuuaAfgUfAfUf ggcaugcagu	3577	PaCfugdCa(Tgn)gccau aCfuUfaagcaau	5058	AUUGCUUAAGUAU GGCAUGCAGC	6539
AD-1948514	gcuuaaguAfUfGfg caugcagcu	3578	PadGcudGcdAugccdA uAfcuuaagcaa	5059	UUGCUUAAGUAUG GCAUGCAGCU	6540
AD-1948515	gcuuaaGfuAfUfGf gcaugcagcu	3579	PaGfcudGc(Agn)ugcca uAfcUfuaagcaa	5060	UUGCUUAAGUAUG GCAUGCAGCU	6541
AD-1948516	cuuaaguaUfGfGfc augcagcuu	3580	PadAgcdTgdCaugcdCa Ufacuuaagca	5061	UGCUUAAGUAUGG CAUGCAGCUG	6542

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948517	uaaguaugGfCfAfugcagcuguu	3581	PadAcadGcdTgcaudGcCfauacuuaag	5062	CUUAAGUAUGGCAUGCAGCUGUA	6543
AD-1948518	uaaguaUfgGfCfAfugcagcuguu	3582	PaAfcadGc(Tgn)gcaugcCfaUfacuuaag	5063	CUUAAGUAUGGCAUGCAGCUGUA	6544
AD-1948519	aaguauggCfAfUfgcagcuguau	3583	PadTacdAgdCugcadTgCfcauacuuaa	5064	UUAAGUAUGGCAUGCAGCUGUAC	6545
AD-1948520	auggcaugCfAfGfcuguaccagu	3584	PadCugdGudAcagcdTgCfaugccauac	5065	GUAUGGCAUGCAGCUGUACCAGA	6546
AD-1948521	uggcaugcAfGfCfuguaccagau	3585	PadTcudGgdTacagdCuGfcaugccaua	5066	UAUGGCAUGCAGCUGUACCAGAA	6547
AD-1948522	uggcauGfcAfGfCfuguaccagau	3586	PaUfcudGg(Tgn)acagcuGfcAfugccaua	5067	UAUGGCAUGCAGCUGUACCAGAA	6548
AD-1948523	ggcaugcaGfCfUfguaccagaau	3587	PadTucdTgdGuacadGcUfgcaugccau	5068	AUGGCAUGCAGCUGUACCAGAAU	6549
AD-1948524	gcaugcagCfUfGfuaccagaauu	3588	PadAuudCudGguacdAgCfugcaugcca	5069	UGGCAUGCAGCUGUACCAGAAUU	6550
AD-1948525	augcagcuGfUfAfccagaauuau	3589	PadTaadTudCuggudAcAfgcugcaugc	5070	GCAUGCAGCUGUACCAGAAUUAU	6551
AD-1948526	ugcagcugUfAfCfcagaauuauu	3590	PadAuadAudTcuggdTaCfagcugcaug	5071	CAUGCAGCUGUACCAGAAUUAUA	6552
AD-1948527	gcagcuguAfCfCfagaauuauau	3591	PadTaudAadTucugdGuAfcagcugcau	5072	AUGCAGCUGUACCAGAAUUAUAU	6553
AD-1948528	cagcuguaCfCfAfgaauuauauu	3592	PadAuadTadAuucudGgUfacagcugca	5073	UGCAGCUGUACCAGAAUUAUAUG	6554
AD-1948529	agcuguacCfAfGfaauuauaugu	3593	PadCaudAudAauucdTgGfuacagcugc	5074	GCAGCUGUACCAGAAUUAUAUGC	6555
AD-1948530	gcuguaccAfGfAfauuauaugcu	3594	PadGcadTadTaauudCuGfguacagcug	5075	CAGCUGUACCAGAAUUAUAUGCA	6556
AD-1948531	cuguaccaGfAfAfuuauaugcau	3595	PadTgcdAudAuaaudTcUfgguacagcu	5076	AGCUGUACCAGAAUUAUAUGCAU	6557
AD-1948532	cuguacCfaGfAfAfuuauaugcau	3596	PaUfgcdAu(Agn)uaauucUfgGfuacagcu	5077	AGCUGUACCAGAAUUAUAUGCAU	6558
AD-1948533	uguaccagAfAfUfuauaugcauu	3597	PadAugdCadTauaadTuCfugguacagc	5078	GCUGUACCAGAAUUAUAUGCAUC	6559
AD-1948534	uguaccAfgAfAfUfuauaugcauu	3598	PaAfugdCa(Tgn)auaauuCfuGfguacagc	5079	GCUGUACCAGAAUUAUAUGCAUC	6560
AD-1948535	guaccagaAfUfUfauaugcaucu	3599	PadGaudGcdAuauadAuUfcugguacag	5080	CUGUACCAGAAUUAUAUGCAUCC	6561
AD-1948536	guaccaGfaAfUfUfauaugcaucu	3600	PaGfaudGc(Agn)uauaauUfcUfgguacag	5081	CUGUACCAGAAUUAUAUGCAUCC	6562
AD-1948537	uaccagaaUfUfAfuaugcauccu	3601	PadGgadTgdCauaudAaUfucugguaca	5082	UGUACCAGAAUUAUAUGCAUCCA	6563
AD-1948538	accagaauUfAfUfaugcauccau	3602	PadTggdAudGcauadTaAfuucugguac	5083	GUACCAGAAUUAUAUGCAUCCAU	6564
AD-1948539	ccagaauuAfUfAfugcauccauu	3603	PadAugdGadTgcaudAuAfauucuggua	5084	UACCAGAAUUAUAUGCAUCCAUA	6565
AD-1948540	ccagaaUfuAfUfAfugcauccauu	3604	PaAfugdGa(Tgn)gcauauAfaUfucuggua	5085	UACCAGAAUUAUAUGCAUCCAUA	6566

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948541	cagaauuaUfAfUfgcauccauau	3605	PadTaudGgdAugcadTaUfaauucuggu	5086	ACCAGAAUUAUAUGCAUCCAUAU	6567
AD-1948542	cagaauUfaUfAfUfgcauccauau	3606	PaUfaudGg(Agn)ugcauaUfaAfuucuggu	5087	ACCAGAAUUAUAUGCAUCCAUAU	6568
AD-1948543	agaauuauAfUfGfcauccauauu	3607	PadAuadTgdGaugcdAuAfuaauucugg	5088	CCAGAAUUAUAUGCAUCCAUAUC	6569
AD-1948544	gaauuauaUfGfCfauccauaucu	3608	PadGaudAudGgaugdCaUfauaauucug	5089	CAGAAUUAUAUGCAUCCAUAUCA	6570
AD-1948545	aauuauauGfCfAfuccauaucau	3609	PadTgadTadTggaudGcAfuauaauucu	5090	AGAAUUAUAUGCAUCCAUAUCAA	6571
AD-1948546	aauuauAfuGfCfAfuccauaucau	3610	PaUfgadTa(Tgn)ggaugcAfuAfuaauucu	5091	AGAAUUAUAUGCAUCCAUAUCAA	6572
AD-1948547	auuauaugCfAfUfccauaucaau	3611	PadTugdAudAuggadTgCfauauaauuc	5092	GAAUUAUAUGCAUCCAUAUCAAG	6573
AD-1948548	uuauaugcAfUfCfcauaucaagu	3612	PadCuudGadTauggdAuGfcauauaauu	5093	AAUUAUAUGCAUCCAUAUCAAGG	6574
AD-1948549	uauaugcaUfCfCfaucaaggu	3613	PadCcudTgdAuaugdGaUfgcauauaau	5094	AUUAUAUGCAUCCAUAUCAAGGU	6575
AD-1948550	uauaugCfaUfCfCfauaucaaggu	3614	PaCfcudTg(Agn)uauggaUfgCfauauaau	5095	AUUAUAUGCAUCCAUAUCAAGGU	6576
AD-1948551	auaugcauCfCfAfuaucaagguu	3615	PadAccdTudGauaudGgAfugcauauaa	5096	UUAUAUGCAUCCAUAUCAAGGUA	6577
AD-1948552	uaugcaucCfAfUfaucaaguau	3616	PadTacdCudTgauadTgGfaugcauaua	5097	UAUAUGCAUCCAUAUCAAGGUAG	6578
AD-1948553	uaugcaUfcCfAfUfaucaaguau	3617	PaUfacdCu(Tgn)gauaugGfaUfgcauaua	5098	UAUAUGCAUCCAUAUCAAGGUAG	6579
AD-1948554	augcauccAfUfAfucaaguagu	3618	PadCuadCcdTugaudAuGfgaugcauau	5099	AUAUGCAUCCAUAUCAAGGUAGA	6580
AD-1948555	ugcauccaUfAfUfcaagguagau	3619	PadTcudAcdCuugadTaUfggaugcaua	5100	UAUGCAUCCAUAUCAAGGUAGAA	6581
AD-1948556	gcauccauAfUfCfaagguagaau	3620	PadTucdTadCcuugdAuAfuggaugcau	5101	AUGCAUCCAUAUCAAGGUAGAAG	6582
AD-1948557	cauccauaUfCfAfagguagaagu	3621	PadCuudCudAccuudGaUfauggaugca	5102	UGCAUCCAUAUCAAGGUAGAAGU	6583
AD-1948558	auccauauCfAfAfgguagaaguu	3622	PadAcudTcdTaccudTgAfuauggaugc	5103	GCAUCCAUAUCAAGGUAGAAGUG	6584
AD-1948559	auccauAfuCfAfAfgguagaaguu	3623	PaAfcudTc(Tgn)accuugAfuAfuggaugc	5104	GCAUCCAUAUCAAGGUAGAAGUG	6585
AD-1948560	uccauaucAfAfGfguagaagugu	3624	PadCacdTudCuaccdTuGfauauggaug	5105	CAUCCAUAUCAAGGUAGAAGUGG	6586
AD-1948561	ccauaucaAfGfGfuagaaguggu	3625	PadCcadCudTcuacdCuUfgauauggau	5106	AUCCAUAUCAAGGUAGAAGUGGC	6587
AD-1948562	gcugcaguUfCfAfcagagcauau	3626	PadTaudGcdTcugudGaAfcugcagcca	5107	UGGCUGCAGUUCACAGAGCAUAU	6588
AD-1948563	gcugcaGfuUfCfAfcagagcauau	3627	PaUfaudGc(Tgn)cugugaAfcUfgcagcca	5108	UGGCUGCAGUUCACAGAGCAUAU	6589
AD-1948564	ugcaguucAfCfAfgagcauaucu	3628	PadGaudAudGcucudGuGfaacugcagc	5109	GCUGCAGUUCACAGAGCAUAUCA	6590

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948565	gcaguucaCfAfGfagcauaucau	3629	PadTgadTadTgcucdTgUfgaacugcag	5110	CUGCAGUUCACAGAGCAUAUCAC	6591
AD-1948566	gcaguuCfaCfAfGfagcauaucau	3630	PaUfgadTa(Tgn)gcucugUfgAfacugcag	5111	CUGCAGUUCACAGAGCAUAUCAC	6592
AD-1948567	accuaugaGfAfAfguauaucagu	3631	PadCugdAudAuacudTcUfcauagguga	5112	UCACCUAUGAGAAGUAUAUCAGA	6593
AD-1948568	ccuaugagAfAfGfuauaucagau	3632	PadTcudGadTauacdTuCfucauaggug	5113	CACCUAUGAGAAGUAUAUCAGAG	6594
AD-1948569	ccuaugAfgAfAfGfuauaucagau	3633	PaUfcudGa(Tgn)auacuuCfuCfauaggug	5114	CACCUAUGAGAAGUAUAUCAGAG	6595
AD-1948570	cuaugagaAfGfUfauaucagagu	3634	PadCucdTgdAuauadCuUfcucauaggu	5115	ACCUAUGAGAAGUAUAUCAGAGA	6596
AD-1948571	cuaugaGfaAfGfUfauaucagagu	3635	PaCfucdTg(Agn)uauacuUfcUfcauaggu	5116	ACCUAUGAGAAGUAUAUCAGAGA	6597
AD-1948572	uaugagaaGfUfAfuaucagagau	3636	PadTcudCudGauaudAcUfucucauagg	5117	CCUAUGAGAAGUAUAUCAGAGAA	6598
AD-1948573	augagaagUfAfUfaucagagaau	3637	PadTucdTcdTgauadTaCfuucucauag	5118	CUAUGAGAAGUAUAUCAGAGAAU	6599
AD-1948574	augagaAfgUfAfUfaucagagaau	3638	PaUfucdTc(Tgn)gauauaCfuUfcucauag	5119	CUAUGAGAAGUAUAUCAGAGAAU	6600
AD-1948575	ccugguagCfAfAfuggacuucuu	3639	PadAgadAgdTccaudTgCfuaccaggga	5120	UCCCUGGUAGCAAUGGACUUCUC	6601
AD-1948576	ccugguAfgCfAfAfuggacuucuu	3640	PaAfgadAg(Tgn)ccauugCfuAfccaggga	5121	UCCCUGGUAGCAAUGGACUUCUC	6602
AD-1948577	caauggacUfUfCfucaggccagu	3641	PadCugdGcdCugagdAaGfuccauugcu	5122	AGCAAUGGACUUCUCAGGCCAGA	6603
AD-1948578	uggacuucUfCfAfggccagaaau	3642	PadTuudCudGgccudGaGfaaguccauu	5123	AAUGGACUUCUCAGGCCAGAAAA	6604
AD-1948579	ggacuucuCfAfGfgccagaaaau	3643	PadTuudTcdTggccdTgAfgaaguccau	5124	AUGGACUUCUCAGGCCAGAAAAG	6605
AD-1948580	ggacuuCfuCfAfGfgccagaaaau	3644	PaUfuudTc(Tgn)ggccugAfgAfaguccau	5125	AUGGACUUCUCAGGCCAGAAAAG	6606
AD-1948581	gacuucucAfGfGfccagaaaagu	3645	PadCuudTudCuggcdCuGfagaagucca	5126	UGGACUUCUCAGGCCAGAAAAGC	6607
AD-1948582	cuucucagGfCfCfagaaaagcau	3646	PadTgcdTudTucugdGcCfugagaaguc	5127	GACUUCUCAGGCCAGAAAAGCAG	6608
AD-1948583	cuucucAfgGfCfCfagaaaagcau	3647	PaUfgcdTu(Tgn)ucuggcCfuGfagaaguc	5128	GACUUCUCAGGCCAGAAAAGCAG	6609
AD-1948584	caggccagAfAfAfagcagaguuu	3648	PadAacdTcdTgcuudTuCfuggccugag	5129	CUCAGGCCAGAAAAGCAGAGUUA	6610
AD-1948585	caggccAfgAfAfAfagcagaguuu	3649	PaAfacdTc(Tgn)gcuuuuCfuGfgccugag	5130	CUCAGGCCAGAAAAGCAGAGUUA	6611
AD-1948586	aggccagaAfAfAfgcagaguuau	3650	PadTaadCudCugcudTuUfcuggccuga	5131	UCAGGCCAGAAAAGCAGAGUUAU	6612
AD-1948587	ggccagaaAfAfGfcagaguuauu	3651	PadAuadAcdTcugcdTuUfucuggccug	5132	CAGGCCAGAAAAGCAGAGUUAUA	6613
AD-1948588	ggccagAfaAfAfGfcagaguuauu	3652	PaAfuadAc(Tgn)cugcuuUfuCfuggccug	5133	CAGGCCAGAAAAGCAGAGUUAUA	6614

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948589	gccagaaaAfGfCfagaguuauau	3653	PadTaudAadCucugdCuUfuucuggccu	5134	AGGCCAGAAAAGCAGAGUUAUAG	6615
AD-1948590	ccagaaaaGfCfAfgaguuauagu	3654	PadCuadTadAcucudGcUfuuucuggcc	5135	GGCCAGAAAAGCAGAGUUAUAGA	6616
AD-1948591	cagaaaagCfAfGfaguuauagau	3655	PadTcudAudAacucdTgCfuuuucuggc	5136	GCCAGAAAAGCAGAGUUAUAGAA	6617
AD-1948592	agaaaagcAfGfAfguuauagaau	3656	PadTucdTadTaacudCuGfcuuuucugg	5137	CCAGAAAAGCAGAGUUAUAGAAA	6618
AD-1948593	agaaaaGfcAfGfAfguuauagaau	3657	PaUfucdTa(Tgn)aacucuGfcUfuuucugg	5138	CCAGAAAAGCAGAGUUAUAGAAA	6619
AD-1948594	gaaaagcaGfAfGfuuauagaaau	3658	PadTuudCudAuaacdTcUfgcuuuucug	5139	CAGAAAAGCAGAGUUAUAGAAAA	6620
AD-1948595	gaaaagCfaGfAfGfuuauagaaau	3659	PaUfuudCu(Agn)uaacucUfgCfuuuucug	5140	CAGAAAAGCAGAGUUAUAGAAAA	6621
AD-1948596	aaaagcagAfGfUfuauagaaaau	3660	PadTuudTcdTauaadCuCfugcuuuucu	5141	AGAAAAGCAGAGUUAUAGAAAAU	6622
AD-1948597	aaaagcAfgAfGfUfuauagaaaau	3661	PaUfuudTc(Tgn)auaacuCfuGfcuuuucu	5142	AGAAAAGCAGAGUUAUAGAAAAU	6623
AD-1948598	aaagcagaGfUfUfauagaaaauu	3662	PadAuudTudCuauadAcUfcugcuuuuc	5143	GAAAAGCAGAGUUAUAGAAAAUC	6624
AD-1948599	aagcagagUfUfAfuagaaaaucu	3663	PadGaudTudTcuaudAaCfucugcuuuu	5144	AAAAGCAGAGUUAUAGAAAAUCC	6625
AD-1948600	aagcagAfgUfUfAfuagaaaaucu	3664	PaGfaudTu(Tgn)cuauaaCfuCfugcuuuu	5145	AAAAGCAGAGUUAUAGAAAAUCC	6626
AD-1948601	agcagaguUfAfUfagaaaauccu	3665	PadGgadTudTucuadTaAfcucugcuuu	5146	AAAGCAGAGUUAUAGAAAAUCCC	6627
AD-1948602	agcagaGfuUfAfUfagaaaauccu	3666	PaGfgadTu(Tgn)ucuauaAfcUfcugcuuu	5147	AAAGCAGAGUUAUAGAAAAUCCC	6628
AD-1948603	gcagaguuAfUfAfgaaaaucccu	3667	PadGggdAudTuucudAuAfacucugcuu	5148	AAGCAGAGUUAUAGAAAAUCCCA	6629
AD-1948604	gcagagUfuAfUfAfgaaaaucccu	3668	PaGfggdAu(Tgn)uucuauAfaCfucugcuu	5149	AAGCAGAGUUAUAGAAAAUCCCA	6630
AD-1948605	cagaguuaUfAfGfaaaaucccau	3669	PadTggdGadTuuucdTaUfaacucugcu	5150	AGCAGAGUUAUAGAAAAUCCCAC	6631
AD-1948606	cagaguUfaUfAfGfaaaaucccau	3670	PaUfggdGa(Tgn)uuucuaUfaAfcucugcu	5151	AGCAGAGUUAUAGAAAAUCCCAC	6632
AD-1948607	agaguuauAfGfAfaaaucccacu	3671	PadGugdGgdAuuuudCuAfuaacucugc	5152	GCAGAGUUAUAGAAAAUCCCACU	6633
AD-1948608	agaguuAfuAfGfAfaaaucccacu	3672	PaGfugdGg(Agn)uuuucuAfuAfacucugc	5153	GCAGAGUUAUAGAAAAUCCCACU	6634
AD-1948609	gaguuauaGfAfAfaaucccacuu	3673	PadAgudGgdGauuudTcUfauaacucug	5154	CAGAGUUAUAGAAAAUCCCACUG	6635
AD-1948610	aguuauagAfAfAfaucccacugu	3674	PadCagdTgdGgauudTuCfuauaacucu	5155	AGAGUUAUAGAAAAUCCCACUGA	6636
AD-1948611	guuauagaAfAfAfucccacugau	3675	PadTcadGudGggaudTuUfcuauaacuc	5156	GAGUUAUAGAAAAUCCCACUGAA	6637
AD-1948612	uuauagaaAfAfUfccacugaau	3676	PadTucdAgdTgggadTuUfucuauaacu	5157	AGUUAUAGAAAAUCCCACUGAAG	6638

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948613	uuauagAfaAfAfUfcccacugaau	3677	PaUfucdAg(Tgn)gggauuUfuCfuauaacu	5158	AGUUAUAGAAAAUCCCACUGAAG	6639
AD-1948614	uauagaaaAfUfCfccacugaagu	3678	PadCuudCadGugggdAuUfuucuauaac	5159	GUUAUAGAAAAUCCCACUGAAGC	6640
AD-1948615	auagaaaaUfCfCfcacugaagcu	3679	PadGcudTcdAguggdGaUfuuucuauaa	5160	UUAUAGAAAAUCCCACUGAAGCC	6641
AD-1948616	auagaaAfaUfCfCfcacugaagcu	3680	PaGfcudTc(Agn)gugggaUfuUfucuauaa	5161	UUAUAGAAAAUCCCACUGAAGCC	6642
AD-1948617	uagaaaauCfCfCfacugaagccu	3681	PadGgcdTudCagugdGgAfuuuucuaua	5162	UAUAGAAAAUCCCACUGAAGCCC	6643
AD-1948618	gaaaauccCfAfCfugaagcccuu	3682	PadAggdGcdTucagdTgGfgauuuucua	5163	UAGAAAAUCCCACUGAAGCCCUU	6644
AD-1948619	gaaaauCfcCfAfCfugaagcccuu	3683	PaAfggdGc(Tgn)ucagugGfgAfuuuucua	5164	UAGAAAAUCCCACUGAAGCCCUU	6645
AD-1948620	aaaaucccAfCfUfgaagcccuuu	3684	PadAagdGgdCuucadGuGfggauuuucu	5165	AGAAAAUCCCACUGAAGCCCUUU	6646
AD-1948621	aaaucccaCfUfGfaagcccuuuu	3685	PadAaadGgdGcuucdAgUfgggauuuuc	5166	GAAAAUCCCACUGAAGCCCUUUC	6647
AD-1948622	ucccacugAfAfGfccuuucagu	3686	PadCugdAadAgggcdTuCfaguggggauu	5167	AAUCCCACUGAAGCCCUUUCAGU	6648
AD-1948623	cccacugaAfGfCfccuuucaguu	3687	PadAcudGadAagggdCuUfcaguggggau	5168	AUCCCACUGAAGCCCUUUCAGUU	6649
AD-1948624	cacugaagCfCfCfuuucaguugu	3688	PadCaadCudGaaagdGgCfuucaguggg	5169	CCCACUGAAGCCCUUUCAGUUGC	6650
AD-1948625	acugaagcCfCfUfuucaguugcu	3689	PadGcadAcdTgaaadGgGfcuucagugg	5170	CCACUGAAGCCCUUUCAGUUGCG	6651
AD-1948626	acugaaGfcCfCfUfuucaguugcu	3690	PaGfcadAc(Tgn)gaaaggGfcUfucagugg	5171	CCACUGAAGCCCUUUCAGUUGCG	6652
AD-1948627	aaggacucGfCfUfuggaggaaau	3691	PadTuudCcdTccaadGcGfaguccuucu	5172	AGAAGGACUCGCUUGGAGGAAAA	6653
AD-1948628	aaggacUfcGfCfUfuggaggaaau	3692	PaUfuudCc(Tgn)ccaagcGfaGfuccuucu	5173	AGAAGGACUCGCUUGGAGGAAAA	6654
AD-1948629	aggacucgCfUfUfggaggaaaau	3693	PadTuudTcdCuccadAgCfgaguccuuc	5174	GAAGGACUCGCUUGGAGGAAAAA	6655
AD-1948630	ggacucgcUfUfGfgaggaaaaau	3694	PadTuudTudCcuccdAaGfcgaguccuu	5175	AAGGACUCGCUUGGAGGAAAAAA	6656
AD-1948631	gacucgcuUfGfGfaggaaaaaau	3695	PadTuudTudTccucdCaAfgcgaguccu	5176	AGGACUCGCUUGGAGGAAAAAAG	6657
AD-1948632	gacucgCfuUfGfGfaggaaaaaau	3696	PaUfuudTu(Tgn)ccuccaAfgCfgaguccu	5177	AGGACUCGCUUGGAGGAAAAAAG	6658
AD-1948633	acucgcuuGfGfAfggaaaaaagu	3697	PadCuudTudTuccudCcAfagcgagucc	5178	GGACUCGCUUGGAGGAAAAAAGG	6659
AD-1948634	cucgcuugGfAfGfgaaaaaaggu	3698	PadCcudTudTuuccdTcCfaagcgaguc	5179	GACUCGCUUGGAGGAAAAAAGGA	6660
AD-1948635	ucgcuuggAfGfGfaaaaaggau	3699	PadTccdTudTuuucdCuCfcaagcgagu	5180	ACUCGCUUGGAGGAAAAAAGGAU	6661
AD-1948636	ucgcuuGfgAfGfGfaaaaaggau	3700	PaUfccdTu(Tgn)uuuccuCfcAfagcgagu	5181	ACUCGCUUGGAGGAAAAAAGGAU	6662

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948637	cgcuuggaGfGfAfaaaaaggauu	3701	PadAucdCudTuuuudCcUfccaagcgag	5182	CUCGCUUGGAGGAAAAAAGGAUG	6663
AD-1948638	gcuuggagGfAfAfaaaaggaugu	3702	PadCaudCcdTuuuudTcCfuccaagcga	5183	UCGCUUGGAGGAAAAAAGGAUGU	6664
AD-1948639	cuuggaggAfAfAfaaaggauguu	3703	PadAcadTcdCuuuudTuCfcuccaagcg	5184	CGCUUGGAGGAAAAAAGGAUGUU	6665
AD-1948640	uuggaggaAfAfAfaaggauguuu	3704	PadAacdAudCcuuudTuUfccuccaagc	5185	GCUUGGAGGAAAAAAGGAUGUUU	6666
AD-1948641	uggaggaaAfAfAfaggauguuuu	3705	PadAaadCadTccuudTuUfuccuccaag	5186	CUUGGAGGAAAAAAGGAUGUUUA	6667
AD-1948642	uggaggAfaAfAfAfaggauguuuu	3706	PaAfaadCa(Tgn)ccuuuuUfuCfcuccaag	5187	CUUGGAGGAAAAAAGGAUGUUUA	6668
AD-1948643	ggaggaaaAfAfAfggauguuuau	3707	PadTaadAcdAuccudTuUfuuccuccaa	5188	UUGGAGGAAAAAAGGAUGUUUAC	6669
AD-1948644	ggaggaAfaAfAfAfggauguuuau	3708	PaUfaadAc(Agn)uccuuuUfuUfccuccaa	5189	UUGGAGGAAAAAAGGAUGUUUAC	6670
AD-1948645	gaggaaaaAfAfGfgauguuuacu	3709	PadGuadAadCauccdTuUfuuccucca	5190	UGGAGGAAAAAAGGAUGUUUACG	6671
AD-1948646	aggaaaaaAfGfGfauguuuacgu	3710	PadCgudAadAcaucdCuUfuuuccucc	5191	GGAGGAAAAAAGGAUGUUUACGC	6672
AD-1948647	ggaaaaaaGfGfAfuguuuacgcu	3711	PadGcgdTadAacaudCcUfuuuuccuc	5192	GAGGAAAAAAGGAUGUUUACGCC	6673
AD-1948648	gaaaaaagGfAfUfguuuacgccu	3712	PadGgcdGudAaacadTcCfuuuuuccu	5193	AGGAAAAAAGGAUGUUUACGCCU	6674
AD-1948649	aaaaaaggAfUfGfuuuacgccuu	3713	PadAggdCgdTaaacdAuCfcuuuuuucc	5194	GGAAAAAAGGAUGUUUACGCCUG	6675
AD-1948650	aaaaaggaUfGfUfuuacgccugu	3714	PadCagdGcdGuaaadCaUfccuuuuuuc	5195	GAAAAAAGGAUGUUUACGCCUGG	6676
AD-1948651	aaaaggauGfUfUfuacgccuggu	3715	PadCcadGgdCguaadAcAfuccuuuuuu	5196	AAAAAAGGAUGUUUACGCCUGGG	6677
AD-1948652	acgccuggGfCfAfcucacgguau	3716	PadTacdCgdTgagudGcCfcaggcguaa	5197	UUACGCCUGGGCACUCACGGUAG	6678
AD-1948653	cacugccuCfUfUfcacagagcuu	3717	PadAgcdTcdTgugadAgAfggcaguggg	5198	CCCACUGCCUCUUCACAGAGCUC	6679
AD-1948654	cacugcCfuCfUfUfcacagagcuu	3718	PaAfgcdTc(Tgn)gugaagAfgGfcaguggg	5199	CCCACUGCCUCUUCACAGAGCUC	6680
AD-1948655	cugccacaAfAfCfauggcuaucu	3719	PadGaudAgdCcaugdTuUfguggcagag	5200	CUCUGCCACAAACAUGGCUAUCC	6681
AD-1948656	ugccacaaAfCfAfuggcuauccu	3720	PadGgadTadGccaudGuUfuguggcaga	5201	UCUGCCACAAACAUGGCUAUCCA	6682
AD-1948657	gccacaaaCfAfUfggcuauccau	3721	PadTggdAudAgccadTgUfuuguggcag	5202	CUGCCACAAACAUGGCUAUCCAC	6683
AD-1948658	gccacaAfaCfAfUfggcuauccau	3722	PaUfggdAu(Agn)gccaugUfuUfguggcag	5203	CUGCCACAAACAUGGCUAUCCAC	6684
AD-1948659	ccacaaacAfUfGfgcuauccacu	3723	PadGugdGadTagccdAuGfuuuguggca	5204	UGCCACAAACAUGGCUAUCCACC	6685
AD-1948660	ccacaaAfcAfUfGfgcuauccacu	3724	PaGfugdGa(Tgn)agccauGfuUfuguggca	5205	UGCCACAAACAUGGCUAUCCACC	6686

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948661	cacaaacaUfGfGfcuauccaccu	3725	PadGgudGgdAuagcdCaUfguuuguggc	5206	GCCACAAACAUGGCUAUCCACCG	6687
AD-1948662	cacaaaCfaUfGfGfcuauccaccu	3726	PaGfgudGg(Agn)uagccaUfgUfuuguggc	5207	GCCACAAACAUGGCUAUCCACCG	6688
AD-1948663	uccaccggUfCfCfcagccauggu	3727	PadCcadTgdGcuggdGaCfcgguggaua	5208	UAUCCACCGGUCCCAGCCAUGGU	6689
AD-1948664	ccaccgguCfCfCfagccaugguu	3728	PadAccdAudGgcugdGgAfccgguggau	5209	AUCCACCGGUCCCAGCCAUGGUU	6690
AD-1948665	caccggucCfCfAfgccaugguuu	3729	PadAacdCadTggcudGgGfaccggugga	5210	UCCACCGGUCCCAGCCAUGGUUU	6691
AD-1948666	caccggUfcCfCfAfgccaugguuu	3730	PaAfacdCa(Tgn)ggcuggGfaCfcggugga	5211	UCCACCGGUCCCAGCCAUGGUUU	6692
AD-1948667	ccggucccAfGfCfcaugguuucu	3731	PadGaadAcdCauggdCuGfggaccggug	5212	CACCGGUCCCAGCCAUGGUUUCA	6693
AD-1948668	gucccagcCfAfUfgguuucaccu	3732	PadGgudGadAaccadTgGfcugggaccg	5213	CGGUCCCAGCCAUGGUUUCACCA	6694
AD-1948669	gucccaGfcCfAfUfgguuucaccu	3733	PaGfgudGa(Agn)accaugGfcUfgggaccg	5214	CGGUCCCAGCCAUGGUUUCACCA	6695
AD-1948670	ucccagccAfUfGfguuucaccau	3734	PadTggdTgdAaaccdAuGfgcugggacc	5215	GGUCCCAGCCAUGGUUUCACCAC	6696
AD-1948671	ucccagCfcAfUfGfguuucaccau	3735	PaUfggdTg(Agn)aaccauGfgCfugggacc	5216	GGUCCCAGCCAUGGUUUCACCAC	6697
AD-1948672	cccagccaUfGfGfuucaccacu	3736	PadGugdGudGaaacdCaUfggcugggac	5217	GUCCCAGCCAUGGUUUCACCACA	6698
AD-1948673	ccagccauGfGfUfucaccacau	3737	PadTgudGgdTgaaadCcAfuggcuggga	5218	UCCCAGCCAUGGUUUCACCACAA	6699
AD-1948674	ccagccAfuGfGfUfuucaccacau	3738	PaUfgudGg(Tgn)gaaaccAfuGfgcuggga	5219	UCCCAGCCAUGGUUUCACCACAA	6700
AD-1948675	cagccaugGfUfUfucaccacaau	3739	PadTugdTgdGugaadAcCfauggcuggg	5220	CCCAGCCAUGGUUUCACCACAAA	6701
AD-1948676	agccauggUfUfUfcaccacaaau	3740	PadTuudGudGgugadAaCfcauggcugg	5221	CCAGCCAUGGUUUCACCACAAAA	6702
AD-1948677	gccaugguUfUfCfaccacaaaau	3741	PadTuudTgdTggugdAaAfccauggcug	5222	CAGCCAUGGUUUCACCACAAAAU	6703
AD-1948678	gccaugGfuUfUfCfaccacaaaau	3742	PaUfuudTg(Tgn)ggugaaAfcCfauggcug	5223	CAGCCAUGGUUUCACCACAAAAU	6704
AD-1948679	ccaugguuUfCfAfccacaaaauu	3743	PadAuudTudGuggudGaAfaccauggcu	5224	AGCCAUGGUUUCACCACAAAAUU	6705
AD-1948680	caugguuuCfAfCfcacaaaauuu	3744	PadAaudTudTguggdTgAfaaccauggc	5225	GCCAUGGUUUCACCACAAAAUUU	6706
AD-1948681	augguuucAfCfCfacaaaauuuu	3745	PadAaadTudTugugdGuGfaaaccaugg	5226	CCAUGGUUUCACCACAAAAUUUC	6707
AD-1948682	ugguuucaCfCfAfcaaaauuucu	3746	PadGaadAudTuugudGgUfgaaaccaug	5227	CAUGGUUUCACCACAAAAUUUCU	6708
AD-1948683	gguuucacCfAfCfaaaauuucuu	3747	PadAgadAadTuuugdTgGfugaaaccau	5228	AUGGUUUCACCACAAAAUUUCUA	6709
AD-1948684	guuucaccAfCfAfaaauuucuau	3748	PadTagdAadAuuuudGuGfgugaaacca	5229	UGGUUUCACCACAAAAUUUCUAG	6710

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948685	uuucaccaCfAfAfaauuucuagu	3749	PadCuadGadAauuudTgUfggugaaacc	5230	GGUUUCACCACAAAAUUUCUAGA	6711
AD-1948686	uucaccacAfAfAfauuucuagau	3750	PadTcudAgdAaauudTuGfuggugaaac	5231	GUUUCACCACAAAAUUUCUAGAG	6712
AD-1948687	ucaccacaAfAfAfuuucuagagu	3751	PadCucdTadGaaaudTuUfguggugaaa	5232	UUUCACCACAAAAUUUCUAGAGA	6713
AD-1948688	caccacaaAfAfUfuucuagagau	3752	PadTcudCudAgaaadTuUfuguggugaa	5233	UUCACCACAAAAUUUCUAGAGAU	6714
AD-1948689	caccacAfaAfAfUfuucuagagau	3753	PaUfcudCu(Agn)gaaauuUfuGfuggugaa	5234	UUCACCACAAAAUUUCUAGAGAU	6715
AD-1948690	accacaaaAfUfUfucuagagauu	3754	PadAucdTcdTagaadAuUfuugugguga	5235	UCACCACAAAAUUUCUAGAGAUG	6716
AD-1948691	accacaAfaAfUfUfucuagagauu	3755	PaAfucdTc(Tgn)agaaauUfuUfuguggua	5236	UCACCACAAAAUUUCUAGAGAUG	6717
AD-1948692	ccacaaaaUfUfUfcuagagaugu	3756	PadCaudCudCuagadAaUfuuuguggug	5237	CACCACAAAAUUUCUAGAGAUGA	6718
AD-1948693	cacaaaauUfUfCfuagagaugau	3757	PadTcadTcdTcuagdAaAfuuuuguggu	5238	ACCACAAAAUUUCUAGAGAUGAG	6719
AD-1948694	cacaaaAfuUfUfCfuagagaugau	3758	PaUfcadTc(Tgn)cuagaaAfuUfuuguggu	5239	ACCACAAAAUUUCUAGAGAUGAG	6720
AD-1948695	acaaaauuUfCfUfagagaugagu	3759	PadCucdAudCucuadGaAfauuuugugg	5240	CCACAAAAUUUCUAGAGAUGAGG	6721
AD-1948696	caaaauuuCfUfAfgagaugaggu	3760	PadCcudCadTcucudAgAfaauuuugug	5241	CACAAAAUUUCUAGAGAUGAGGC	6722
AD-1948697	aaaauuucUfAfGfagaugaggcu	3761	PadGccdTcdAucucdTaGfaaauuuugu	5242	ACAAAAUUUCUAGAGAUGAGGCU	6723
AD-1948698	aaaauuUfcUfAfGfagaugaggcu	3762	PaGfccdTc(Agn)ucucuaGfaAfauuuugu	5243	ACAAAAUUUCUAGAGAUGAGGCU	6724
AD-1948699	aaauuucuAfGfAfgaugaggcuu	3763	PadAgcdCudCaucudCuAfgaaauuuug	5244	CAAAAUUUCUAGAGAUGAGGCUC	6725
AD-1948700	aauuucuaGfAfGfaugaggcucu	3764	PadGagdCcdTcaucdTcUfagaaauuuu	5245	AAAAUUUCUAGAGAUGAGGCUCA	6726
AD-1948701	aauuucUfaGfAfGfaugaggcucu	3765	PaGfagdCc(Tgn)caucucUfaGfaaauuuu	5246	AAAAUUUCUAGAGAUGAGGCUCA	6727
AD-1948702	auuucuagAfGfAfugaggcucau	3766	PadTgadGcdCucaudCuCfuagaaauuu	5247	AAAUUUCUAGAGAUGAGGCUCAG	6728
AD-1948703	uagagaugAfGfGfcucagcgauu	3767	PadAucdGcdTgagcdCuCfaucucuaga	5248	UCUAGAGAUGAGGCUCAGCGAUU	6729
AD-1948704	agagaugaGfGfCfucagcgauuu	3768	PadAaudCgdCugagdCcUfcaucucuag	5249	CUAGAGAUGAGGCUCAGCGAUUG	6730
AD-1948705	gaugaggcUfCfAfgcgauugauu	3769	PadAucdAadTcgcudGaGfccucaucuc	5250	GAGAUGAGGCUCAGCGAUUGAUU	6731
AD-1948706	gaugagGfcUfCfAfgcgauugauu	3770	PaAfucdAa(Tgn)cgcugaGfcCfucaucuc	5251	GAGAUGAGGCUCAGCGAUUGAUU	6732
AD-1948707	augaggcuCfAfGfcgauugauuu	3771	PadAaudCadAucgcdTgAfgccucaucu	5252	AGAUGAGGCUCAGCGAUUGAUUA	6733
AD-1948708	ugaggcucAfGfCfgauugauuau	3772	PadTaadTcdAaucgdCuGfagccucauc	5253	GAUGAGGCUCAGCGAUUGAUUAU	6734

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948709	ugaggcUfcAfGfCfgauugauuau	3773	PaUfaadTc(Agn)aucgcuGfaGfccucauc	5254	GAUGAGGCUCAGCGAUUGAUUAU	6735
AD-1948710	gaggcucaGfCfGfauugauuauu	3774	PadAuadAudCaaucdGcUfgagccucau	5255	AUGAGGCUCAGCGAUUGAUUAUU	6736
AD-1948711	aggcucagCfGfAfuugauuauuu	3775	PadAaudAadTcaaudCgCfugagccuca	5256	UGAGGCUCAGCGAUUGAUUAUUC	6737
AD-1948712	ggcucagcGfAfUfugauuauucu	3776	PadGaadTadAucaadTcGfcugagccuc	5257	GAGGCUCAGCGAUUGAUUAUUCA	6738
AD-1948713	gcucagcgAfUfUfgauuauucau	3777	PadTgadAudAaucadAuCfgcugagccu	5258	AGGCUCAGCGAUUGAUUAUUCAG	6739
AD-1948714	cucagcgaUfUfGfauuauucagu	3778	PadCugdAadTaaucdAaUfcgcugagcc	5259	GGCUCAGCGAUUGAUUAUUCAGC	6740
AD-1948715	ucagcgauUfGfAfuuauucagcu	3779	PadGcudGadAuaaudCaAfucgcugagc	5260	GCUCAGCGAUUGAUUAUUCAGCA	6741
AD-1948716	ucagcgAfuUfGfAfuuauucagcu	3780	PaGfcudGa(Agn)uaaucaAfuCfgcugagc	5261	GCUCAGCGAUUGAUUAUUCAGCA	6742
AD-1948717	cagcgauuGfAfUfuauucagcau	3781	PadTgcdTgdAauaadTcAfaucgcugag	5262	CUCAGCGAUUGAUUAUUCAGCAA	6743
AD-1948718	cagcgaUfuGfAfUfuauucagcau	3782	PaUfgcdTg(Agn)auaaucAfaUfcgcugag	5263	CUCAGCGAUUGAUUAUUCAGCAA	6744
AD-1948719	agcgauugAfUfUfauucagcaau	3783	PadTugdCudGaauadAuCfaaucgcuga	5264	UCAGCGAUUGAUUAUUCAGCAAG	6745
AD-1948720	gcgauugaUfUfAfuucagcaagu	3784	PadCuudGcdTgaaudAaUfcaaucgcug	5265	CAGCGAUUGAUUAUUCAGCAAGG	6746
AD-1948721	gcgauuGfaUfUfAfuucagcaagu	3785	PaCfuudGc(Tgn)gaauaaUfcAfaucgcug	5266	CAGCGAUUGAUUAUUCAGCAAGG	6747
AD-1948722	cgauugauUfAfUfucagcaaggu	3786	PadCcudTgdCugaadTaAfucaaucgcu	5267	AGCGAUUGAUUAUUCAGCAAGGA	6748
AD-1948723	gauugauuAfUfUfcagcaaggau	3787	PadTccdTudGcugadAuAfaucaaucgc	5268	GCGAUUGAUUAUUCAGCAAGGAC	6749
AD-1948724	auugauuaUfUfCfagcaaggacu	3788	PadGucdCudTgcugdAaUfaaucaaucg	5269	CGAUUGAUUAUUCAGCAAGGACU	6750
AD-1948725	auugauUfaUfUfCfagcaaggacu	3789	PaGfucdCu(Tgn)gcugaaUfaAfucaaucg	5270	CGAUUGAUUAUUCAGCAAGGACU	6751
AD-1948726	uugauuauUfCfAfgcaaggacuu	3790	PadAgudCcdTugcudGaAfuaaucaauc	5271	GAUUGAUUAUUCAGCAAGGACUU	6752
AD-1948727	uugauuAfuUfCfAfgcaaggacuu	3791	PaAfgudCc(Tgn)ugcugaAfuAfaucaauc	5272	GAUUGAUUAUUCAGCAAGGACUU	6753
AD-1948728	ugauuauuCfAfGfcaaggacuuu	3792	PadAagdTcdCuugcdTgAfauaaucaau	5273	AUUGAUUAUUCAGCAAGGACUUG	6754
AD-1948729	gauuauucAfGfCfaaggacuugu	3793	PadCaadGudCcuugdCuGfaauaaucaa	5274	UUGAUUAUUCAGCAAGGACUUGU	6755
AD-1948730	auuauucaGfCfAfaggacuuguu	3794	PadAcadAgdTccuudGcUfgaauaauca	5275	UGAUUAUUCAGCAAGGACUUGUG	6756
AD-1948731	auuauuCfaGfCfAfaggacuuguu	3795	PaAfcadAg(Tgn)ccuugcUfgAfauaauca	5276	UGAUUAUUCAGCAAGGACUUGUG	6757
AD-1948732	uuauucagCfAfAfggacuugugu	3796	PadCacdAadGuccudTgCfugaauaauc	5277	GAUUAUUCAGCAAGGACUUGUGG	6758

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948733	uauucagcAfAfGfg acuuguggu	3797	PadCcadCadAgucdTu Gfcugaauaau	5278	AUUAUUCAGCAAG GACUUGUGGA	6759
AD-1948734	auucagcaAfGfGfac uuguggau	3798	PadTccdAcdAagucdCu Ufgcugaauaa	5279	UUAUUCAGCAAGG ACUUGUGGAU	6760
AD-1948735	uucagcaaGfGfAfc uuguggauu	3799	PadAucdCadCaagudCc Ufugcugaaua	5280	UAUUCAGCAAGGA CUUGUGGAUG	6761
AD-1948736	gcaaggacUfUfGfu ggauggagu	3800	PadCucdCadTccacdAa Gfuccuugcug	5281	CAGCAAGGACUUG UGGAUGGAGU	6762
AD-1948737	caaggacuUfGfUfg gauggaguu	3801	PadAcudCcdAuccadCa Afguccuugcu	5282	AGCAAGGACUUGU GGAUGGAGUU	6763
AD-1948738	caaggaCfuUfGfUf ggauggaguu	3802	PaAfcudCc(Agn)uccac aAfgUfccuugcu	5283	AGCAAGGACUUGU GGAUGGAGUU	6764
AD-1948739	aggacuugUfGfGfa uggaguuuu	3803	PadAaadCudCcaucdCa Cfaaguccuug	5284	CAAGGACUUGUGG AUGGAGUUUU	6765
AD-1948740	ggacuuguGfGfAfu ggaguuuuu	3804	PadAaadAcdTccaudCc Afcaaguccuu	5285	AAGGACUUGUGGA UGGAGUUUUC	6766
AD-1948741	ggacuuGfuGfGfAf uggaguuuuu	3805	PaAfaadAc(Tgn)ccauc cAfcAfaguccuu	5286	AAGGACUUGUGGA UGGAGUUUUC	6767
AD-1948742	gacuugugGfAfUfg gaguuuucu	3806	PadGaadAadCuccadTc Cfacaaguccu	5287	AGGACUUGUGGAU GGAGUUUUCU	6768
AD-1948743	acuuguggAfUfGfg aguuuucuu	3807	PadAgadAadAcuccdA uCfcacaagucc	5288	GGACUUGUGGAUG GAGUUUUCUU	6769
AD-1948744	cuuguggaUfGfGfa guuuucuuu	3808	PadAagdAadAacucdC aUfccacaaguc	5289	GACUUGUGGAUGG AGUUUUCUUG	6770
AD-1948745	uuguggauGfGfAfg uuuucuugu	3809	PadCaadGadAaacudCc Afuccacaagu	5290	ACUUGUGGAUGGA GUUUUCUUGG	6771
AD-1948746	uguggaugGfAfGfu uuucuuggu	3810	PadCcadAgdAaaacdTc Cfauccacaag	5291	CUUGUGGAUGGAG UUUUCUUGGU	6772
AD-1948747	guggauggAfGfUfu uucuugguu	3811	PadAccdAadGaaaadCu Cfcauccacaa	5292	UUGUGGAUGGAGU UUUCUUGGUA	6773
AD-1948748	uggauggaGfUfUfu ucuugguau	3812	PadTacdCadAgaaadAc Ufccauccaca	5293	UGUGGAUGGAGUU UUCUUGGUAC	6774
AD-1948749	uggaugGfaGfUfUf uucuugguau	3813	PaUfacdCa(Agn)gaaaa cUfcCfauccaca	5294	UGUGGAUGGAGUU UUCUUGGUAC	6775
AD-1948750	ggauggagUfUfUfu cuugguacu	3814	PadGuadCcdAagaadA aCfuccauccac	5295	GUGGAUGGAGUUU UCUUGGUACG	6776
AD-1948751	gauggaguUfUfUfc uugguacgu	3815	PadCgudAcdCaagadA aAfcuccaucca	5296	UGGAUGGAGUUUU CUUGGUACGG	6777
AD-1948752	auggaguuUfUfCfu ugguacggu	3816	PadCcgdTadCcaagdAa Afacuccaucc	5297	GGAUGGAGUUUUC UUGGUACGGG	6778
AD-1948753	uggaguuuUfCfUfu gguacgggu	3817	PadCccdGudAccaadGa Afaacuccauc	5298	GAUGGAGUUUUCU UGGUACGGGA	6779
AD-1948754	gaguuuucUfUfGfg uacgggauu	3818	PadAucdCcdGuaccdA aGfaaaacucca	5299	UGGAGUUUUCUUG GUACGGGAUA	6780
AD-1948755	aguuuucuUfGfGfu acgggauau	3819	PadTaudCcdCguacdCa Afgaaaacucc	5300	GGAGUUUUCUUGG UACGGGAUAG	6781
AD-1948756	guuuucuuGfGfUfa cgggauagu	3820	PadCuadTcdCcguadCc Afagaaaacuc	5301	GAGUUUUCUUGGU ACGGGAUAGU	6782

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948757	uuuucuugGfUfAfcgggauaguu	3821	PadAcudAudCccgudAcCfaagaaaacu	5302	AGUUUUCUUGGUACGGGAUAGUC	6783
AD-1948758	uuucuuggUfAfCfggauagucu	3822	PadGacdTadTcccgdTaCfcaagaaaac	5303	GUUUUCUUGGUACGGGAUAGUCA	6784
AD-1948759	uuucuuGfgUfAfCfgggauagucu	3823	PaGfacdTa(Tgn)cccguaCfcAfagaaaac	5304	GUUUUCUUGGUACGGGAUAGUCA	6785
AD-1948760	uucuugguAfCfGfggauagucau	3824	PadTgadCudAucccdGuAfccaagaaaa	5305	UUUUCUUGGUACGGGAUAGUCAG	6786
AD-1948761	uucuugGfuAfCfGfggauagucau	3825	PaUfgadCu(Agn)ucccguAfcCfaagaaaa	5306	UUUUCUUGGUACGGGAUAGUCAG	6787
AD-1948762	ucuugguaCfGfGfgauagucagu	3826	PadCugdAcdTauccdCgUfaccaagaaa	5307	UUUCUUGGUACGGGAUAGUCAGA	6788
AD-1948763	ucuuggUfaCfGfGfgauagucagu	3827	PaCfugdAc(Tgn)aucccgUfaCfcaagaaa	5308	UUUCUUGGUACGGGAUAGUCAGA	6789
AD-1948764	cuugguacGfGfGfauagucagau	3828	PadTcudGadCuaucdCcGfuaccaagaa	5309	UUCUUGGUACGGGAUAGUCAGAG	6790
AD-1948765	uugguacgGfGfAfuagucagagu	3829	PadCucdTgdAcuaudCcCfguaccaaga	5310	UCUUGGUACGGGAUAGUCAGAGU	6791
AD-1948766	uugguaCfgGfGfAfuagucagagu	3830	PaCfucdTg(Agn)cuauccCfgUfaccaaga	5311	UCUUGGUACGGGAUAGUCAGAGU	6792
AD-1948767	ugguacggGfAfUfagucagaguu	3831	PadAcudCudGacuadTcCfcguaccaag	5312	CUUGGUACGGGAUAGUCAGAGUA	6793
AD-1948768	gguacgggAfUfAfgucagaguau	3832	PadTacdTcdTgacudAuCfccguaccaa	5313	UUGGUACGGGAUAGUCAGAGUAA	6794
AD-1948769	gguacgGfgAfUfAfgucagaguau	3833	PaUfacdTc(Tgn)gacuauCfcCfguaccaa	5314	UUGGUACGGGAUAGUCAGAGUAA	6795
AD-1948770	guacgggaUfAfGfucagaguaau	3834	PadTuadCudCugacdTaUfcccguacca	5315	UGGUACGGGAUAGUCAGAGUAAC	6796
AD-1948771	uacgggauAfGfUfcagaguaacu	3835	PadGuudAcdTcugadCuAfucccguacc	5316	GGUACGGGAUAGUCAGAGUAACC	6797
AD-1948772	uacgggAfuAfGfUfcagaguaacu	3836	PaGfuudAc(Tgn)cugacuAfuCfccguacc	5317	GGUACGGGAUAGUCAGAGUAACC	6798
AD-1948773	acgggauaGfUfCfagaguaaccu	3837	PadGgudTadCucugdAcUfaucccguac	5318	GUACGGGAUAGUCAGAGUAACCC	6799
AD-1948774	caaaacuuUfCfGfuacugucaau	3838	PadTugdAcdAguacdGaAfaguuuuggg	5319	CCCAAAACUUUCGUACUGUCAAU	6800
AD-1948775	caaaacUfuUfCfGfuacugucaau	3839	PaUfugdAc(Agn)guacgaAfaGfuuuuggg	5320	CCCAAAACUUUCGUACUGUCAAU	6801
AD-1948776	aaaacuuuCfGfUfacugucaauu	3840	PadAuudGadCaguadCgAfaaguuuugg	5321	CCAAAACUUUCGUACUGUCAAUG	6802
AD-1948777	aaacuuucGfUfAfcugucaaugu	3841	PadCaudTgdAcagudAcGfaaaguuuug	5322	CAAAACUUUCGUACUGUCAAUGA	6803
AD-1948778	aaacuuUfcGfUfAfcugucaaugu	3842	PaCfaudTg(Agn)caguacGfaAfaguuuug	5323	CAAAACUUUCGUACUGUCAAUGA	6804
AD-1948779	aacuuucgUfAfCfugucaaugau	3843	PadTcadTudGacagdTaCfgaaaguuuu	5324	AAAACUUUCGUACUGUCAAUGAG	6805
AD-1948780	acuuucguAfCfUfgucaaugagu	3844	PadCucdAudTgacadGuAfcgaaaguuu	5325	AAACUUUCGUACUGUCAAUGAGU	6806

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948781	cuuucguaCfUfGfucaaugaguu	3845	PadAcudCadTugacdAgUfacgaaaguu	5326	AACUUUCGUACUGUCAAUGAGUC	6807
AD-1948782	cuuucgUfaCfUfGfucaaugaguu	3846	PaAfcudCa(Tgn)ugacagUfaCfgaaaguu	5327	AACUUUCGUACUGUCAAUGAGUC	6808
AD-1948783	uuucguacUfGfUfcaaugagucu	3847	PadGacdTcdAuugadCaGfuacgaaagu	5328	ACUUUCGUACUGUCAAUGAGUCA	6809
AD-1948784	uuucguAfcUfGfUfcaaugagucu	3848	PaGfacdTc(Agn)uugacaGfuAfcgaaagu	5329	ACUUUCGUACUGUCAAUGAGUCA	6810
AD-1948785	uucguacuGfUfCfaaugagucau	3849	PadTgadCudCauugdAcAfguacgaaag	5330	CUUUCGUACUGUCAAUGAGUCAU	6811
AD-1948786	ucguacugUfCfAfaugagucauu	3850	PadAugdAcdTcauudGaCfaguacgaaa	5331	UUUCGUACUGUCAAUGAGUCAUG	6812
AD-1948787	ucguacUfgUfCfAfaugagucauu	3851	PaAfugdAc(Tgn)cauugaCfaGfuacgaaa	5332	UUUCGUACUGUCAAUGAGUCAUG	6813
AD-1948788	cguacuguCfAfAfugagucaugu	3852	PadCaudGadCucaudTgAfcaguacgaa	5333	UUCGUACUGUCAAUGAGUCAUGG	6814
AD-1948789	guacugucAfAfUfgagucauggu	3853	PadCcadTgdAcucadTuGfacaguacga	5334	UCGUACUGUCAAUGAGUCAUGGA	6815
AD-1948790	guacugUfcAfAfUfgagucauggu	3854	PaCfcadTg(Agn)cucauuGfaCfaguacga	5335	UCGUACUGUCAAUGAGUCAUGGA	6816
AD-1948791	uacugucaAfUfGfagucauggau	3855	PadTccdAudGacucdAuUfgacaguacg	5336	CGUACUGUCAAUGAGUCAUGGAC	6817
AD-1948792	acugucaaUfGfAfgucauggacu	3856	PadGucdCadTgacudCaUfugacaguac	5337	GUACUGUCAAUGAGUCAUGGACA	6818
AD-1948793	acugucAfaUfGfAfgucauggacu	3857	PaGfucdCa(Tgn)gacucaUfuGfacaguac	5338	GUACUGUCAAUGAGUCAUGGACA	6819
AD-1948794	cugucaauGfAfGfucauggacau	3858	PadTgudCcdAugacdTcAfuugacagua	5339	UACUGUCAAUGAGUCAUGGACAA	6820
AD-1948795	cugucaAfuGfAfGfucauggacau	3859	PaUfgudCc(Agn)ugacucAfuUfgacagua	5340	UACUGUCAAUGAGUCAUGGACAA	6821
AD-1948796	ugucaaugAfGfUfcauggacaau	3860	PadTugdTcdCaugadCuCfauugacagu	5341	ACUGUCAAUGAGUCAUGGACAAA	6822
AD-1948797	gucaaugaGfUfCfauggacaaau	3861	PadTuudGudCcaugdAcUfcauugacag	5342	CUGUCAAUGAGUCAUGGACAAAA	6823
AD-1948798	ucaaugagUfCfAfuggacaaaau	3862	PadTuudTgdTccaudGaCfucauugaca	5343	UGUCAAUGAGUCAUGGACAAAAA	6824
AD-1948799	ucaaugAfgUfCfAfuggacaaaau	3863	PaUfuudTg(Tgn)ccaugaCfuCfauugaca	5344	UGUCAAUGAGUCAUGGACAAAAA	6825
AD-1948800	caaugaguCfAfUfggacaaaaau	3864	PadTuudTudGuccadTgAfcucauugac	5345	GUCAAUGAGUCAUGGACAAAAAA	6826
AD-1948801	aaugagucAfUfGfgacaaaaaau	3865	PadTuudTudTguccdAuGfacucauuga	5346	UCAAUGAGUCAUGGACAAAAAAU	6827
AD-1948802	aaugagUfcAfUfGfgacaaaaaau	3866	PaUfuudTu(Tgn)guccauGfaCfucauuga	5347	UCAAUGAGUCAUGGACAAAAAAU	6828
AD-1948803	augagucaUfGfGfacaaaaaauu	3867	PadAuudTudTugucdCaUfgacucauug	5348	CAAUGAGUCAUGGACAAAAAAUA	6829
AD-1948804	augaguCfaUfGfGfacaaaaaauu	3868	PaAfuudTu(Tgn)ugucccaUfgAfcucauug	5349	CAAUGAGUCAUGGACAAAAAAUA	6830

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948805	ugagucauGfGfAfcaaaaaauau	3869	PadTaudTudTuugudCcAfugacucauu	5350	AAUGAGUCAUGGACAAAAAAUAA	6831
AD-1948806	ugagucAfuGfGfAfcaaaaaauau	3870	PaUfaudTu(Tgn)uuguccAfuGfacucauu	5351	AAUGAGUCAUGGACAAAAAAUAA	6832
AD-1948807	gagucaugGfAfCfaaaaaauaau	3871	PadTuadTudTuuugdTcCfaugacucau	5352	AUGAGUCAUGGACAAAAAAUAAA	6833
AD-1948808	gagucaUfgGfAfCfaaaaaauaau	3872	PaUfuadTu(Tgn)uuugucCfaUfgacucau	5353	AUGAGUCAUGGACAAAAAAUAAA	6834
AD-1948809	agucauggAfCfAfaaaaauaaau	3873	PadTuudAudTuuuudGuCfcaugacuca	5354	UGAGUCAUGGACAAAAAAUAAAG	6835
AD-1948810	agucauGfgAfCfAfaaaaauaaau	3874	PaUfuudAu(Tgn)uuuuguCfcAfugacuca	5355	UGAGUCAUGGACAAAAAAUAAAG	6836
AD-1948811	gucauggaCfAfAfaaaauaaagu	3875	PadCuudTadTuuuudTgUfccaugacuc	5356	GAGUCAUGGACAAAAAAUAAAGC	6837
AD-1948812	ucauggacAfAfAfaaauaaagcu	3876	PadGcudTudAuuuudTuGfuccaugacu	5357	AGUCAUGGACAAAAAAUAAAGCA	6838
AD-1948813	cauggacaAfAfAfaauaaagcau	3877	PadTgcdTudTauuudTuUfguccaugac	5358	GUCAUGGACAAAAAAUAAAGCAC	6839
AD-1948814	cauggaCfaAfAfAfaauaaagcau	3878	PaUfgcdTu(Tgn)auuuuuUfgUfccaugac	5359	GUCAUGGACAAAAAAUAAAGCAC	6840
AD-1948815	auggacaaAfAfAfauaaagcacu	3879	PadGugdCudTuauudTuUfuguccauga	5360	UCAUGGACAAAAAAUAAAGCACU	6841
AD-1948816	auggacAfaAfAfAfauaaagcacu	3880	PaGfugdCu(Tgn)uauuuuUfuGfuccauga	5361	UCAUGGACAAAAAAUAAAGCACU	6842
AD-1948817	uggacaaaAfAfAfuaaagcacuu	3881	PadAgudGcdTuuaudTuUfuuguccaug	5362	CAUGGACAAAAAAUAAAGCACUU	6843
AD-1948818	uggacaAfaAfAfAfuaaagcacuu	3882	PaAfgudGc(Tgn)uuauuuUfuUfguccaug	5363	CAUGGACAAAAAAUAAAGCACUU	6844
AD-1948819	ggacaaaaAfAfUfaaagcacuuu	3883	PadAagdTgdCuuuadTuUfuuuguccau	5364	AUGGACAAAAAAUAAAGCACUUU	6845
AD-1948820	gacaaaaaAfUfAfaagcacuuuu	3884	PadAaadGudGcuuudAuUfuuuugucca	5365	UGGACAAAAAAUAAAGCACUUUC	6846
AD-1948821	acaaaaaUfAfAfagcacuuucu	3885	PadGaadAgdTgcuudTaUfuuuuugucc	5366	GGACAAAAAAUAAAGCACUUUCA	6847
AD-1948822	acaaaAfaUfAfAfagcacuuucu	3886	PaGfaadAg(Tgn)gcuuuaUfuUfuuugucc	5367	GGACAAAAAAUAAAGCACUUUCA	6848
AD-1948823	caaaaauAfAfAfgcacuuucau	3887	PadTgadAadGugcudTuAfuuuuuuguc	5368	GACAAAAAAUAAAGCACUUUCAA	6849
AD-1948824	aaagcacuUfUfCfaaauuauacu	3888	PadGuadTadAuuugdAaAfgugcuuuau	5369	AUAAAGCACUUUCAAAUUAUACC	6850
AD-1948825	aagcacuuUfCfAfaauuauaccu	3889	PadGgudAudAauuudGaAfagugcuuua	5370	UAAAGCACUUUCAAAUUAUACCA	6851
AD-1948826	agcacuuuCfAfAfauuauaccau	3890	PadTggdTadTaauudTgAfaagugcuuu	5371	AAAGCACUUUCAAAUUAUACCAG	6852
AD-1948827	agcacuUfuCfAfAfauuauaccau	3891	PaUfggdTa(Tgn)aauuugAfaAfgugcuuu	5372	AAAGCACUUUCAAAUUAUACCAG	6853
AD-1948828	gcacuuucAfAfAfuuauaccagu	3892	PadCugdGudAuaaudTuGfaaagugcuu	5373	AAGCACUUUCAAAUUAUACCAGU	6854

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948829	cacuuucaAfAfUfuauaccaguu	3893	PadAcudGgdTauaadTuUfgaaagugcu	5374	AGCACUUUCAAAUUAUACCAGUA	6855
AD-1948830	cacuuuCfaAfAfUfuauaccaguu	3894	PaAfcudGg(Tgn)auaauuUfgAfaagugcu	5375	AGCACUUUCAAAUUAUACCAGUA	6856
AD-1948831	acuuucaaAfUfUfauaccaguau	3895	PadTacdTgdGuauadAuUfugaaagugc	5376	GCACUUUCAAAUUAUACCAGUAG	6857
AD-1948832	cuuucaaaUfUfAfuaccaguagu	3896	PadCuadCudGguaudAaUfuugaaagug	5377	CACUUUCAAAUUAUACCAGUAGA	6858
AD-1948833	uuucaaauUfAfUfaccaguagau	3897	PadTcudAcdTgguadTaAfuuugaaagu	5378	ACUUUCAAAUUAUACCAGUAGAA	6859
AD-1948834	uuucaaAfuUfAfUfaccaguagau	3898	PaUfcudAc(Tgn)gguauaAfuUfugaaagu	5379	ACUUUCAAAUUAUACCAGUAGAA	6860
AD-1948835	uucaaauuAfUfAfccaguagaau	3899	PadTucdTadCuggudAuAfauuugaaag	5380	CUUUCAAAUUAUACCAGUAGAAG	6861
AD-1948836	ucaaauuaUfAfCfcaguagaagu	3900	PadCuudCudAcuggdTaUfaauuugaaa	5381	UUUCAAAUUAUACCAGUAGAAGA	6862
AD-1948837	caaauuauAfCfCfaguagaagau	3901	PadTcudTcdTacugdGuAfuaauuugaa	5382	UUCAAAUUAUACCAGUAGAAGAU	6863
AD-1948838	caaauuAfuAfCfCfaguagaagau	3902	PaUfcudTc(Tgn)acugguAfuAfauuugaa	5383	UUCAAAUUAUACCAGUAGAAGAU	6864
AD-1948839	aaauuauaCfCfAfguagaagauu	3903	PadAucdTudCuacudGgUfauaauuuga	5384	UCAAAUUAUACCAGUAGAAGAUG	6865
AD-1948840	aauuauacCfAfGfuagaagaugu	3904	PadCaudCudTcuacdTgGfuauaauuug	5385	CAAAUUAUACCAGUAGAAGAUGA	6866
AD-1948841	auuauaccAfGfUfagaagaugau	3905	PadTcadTcdTucuadCuGfguauaauuu	5386	AAAUUAUACCAGUAGAAGAUGAC	6867
AD-1948842	auuauaCfcAfGfUfagaagaugau	3906	PaUfcadTc(Tgn)ucuacuGfgUfauaauuu	5387	AAAUUAUACCAGUAGAAGAUGAC	6868
AD-1948843	uuauaccaGfUfAfgaagaugacu	3907	PadGucdAudCuucudAcUfgguauaauu	5388	AAUUAUACCAGUAGAAGAUGACG	6869
AD-1948844	uauaccagUfAfGfaagaugacgu	3908	PadCgudCadTcuucdTaCfugguauaau	5389	AUUAUACCAGUAGAAGAUGACGG	6870
AD-1948845	uauaccAfgUfAfGfaagaugacgu	3909	PaCfgudCa(Tgn)cuucuaCfuGfguauaau	5390	AUUAUACCAGUAGAAGAUGACGG	6871
AD-1948846	uaccaguaGfAfAfgaugacgguu	3910	PadAccdGudCaucudTcUfacugguaua	5391	UAUACCAGUAGAAGAUGACGGUG	6872
AD-1948847	accaguagAfAfGfaugacggugu	3911	PadCacdCgdTcaucdTuCfuacugguau	5392	AUACCAGUAGAAGAUGACGGUGA	6873
AD-1948848	ccaguagaAfGfAfugacggugau	3912	PadTcadCcdGucaudCuUfcuacuggua	5393	UACCAGUAGAAGAUGACGGUGAA	6874
AD-1948849	caguagaaGfAfUfgacggugaau	3913	PadTucdAcdCgucadTcUfucuacuggu	5394	ACCAGUAGAAGAUGACGGUGAAA	6875
AD-1948850	aguagaagAfUfGfacggugaaau	3914	PadTuudCadCcgucdAuCfuucuacugg	5395	CCAGUAGAAGAUGACGGUGAAAU	6876
AD-1948851	guagaagaUfGfAfcggugaaauu	3915	PadAuudTcdAccgudCaUfcuucuacug	5396	CAGUAGAAGAUGACGGUGAAAUG	6877
AD-1948852	guagaaGfaUfGfAfcggugaaauu	3916	PaAfuudTc(Agn)ccgucaUfcUfucuacug	5397	CAGUAGAAGAUGACGGUGAAAUG	6878

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948853	uagaagauGfAfCfggugaaaugu	3917	PadCaudTudCaccgdTcAfucuucuacu	5398	AGUAGAAGAUGACGGUGAAAUGU	6879
AD-1948854	agaagaugAfCfGfgugaaauguu	3918	PadAcadTudTcaccdGuCfaucuucuac	5399	GUAGAAGAUGACGGUGAAAUGUU	6880
AD-1948855	agaagaUfgAfCfGfgugaaauguu	3919	PaAfcadTu(Tgn)caccguCfaUfcuucuac	5400	GUAGAAGAUGACGGUGAAAUGUU	6881
AD-1948856	gaagaugaCfGfGfugaaauguuu	3920	PadAacdAudTucacdCgUfcaucuucua	5401	UAGAAGAUGACGGUGAAAUGUUC	6882
AD-1948857	aagaugacGfGfUfgaaauguucu	3921	PadGaadCadTuucadCcGfucaucuucu	5402	AGAAGAUGACGGUGAAAUGUUCC	6883
AD-1948858	aagaugAfcGfGfUfgaaauguucu	3922	PaGfaadCa(Tgn)uucaccGfuCfaucuucu	5403	AGAAGAUGACGGUGAAAUGUUCC	6884
AD-1948859	agaugacgGfUfGfaaauguuccu	3923	PadGgadAcdAuuucdAcCfgucaucuuc	5404	GAAGAUGACGGUGAAAUGUUCCA	6885
AD-1948860	agaugaCfgGfUfGfaaauguuccu	3924	PaGfgadAc(Agn)uuucacCfgUfcaucuuc	5405	GAAGAUGACGGUGAAAUGUUCCA	6886
AD-1948861	gaugacggUfGfAfaauguuccau	3925	PadTggdAadCauuudCaCfcgucaucuu	5406	AAGAUGACGGUGAAAUGUUCCAC	6887
AD-1948862	augacgguGfAfAfauguuccacu	3926	PadGugdGadAcauudTcAfccgucaucu	5407	AGAUGACGGUGAAAUGUUCCACA	6888
AD-1948863	augacgGfuGfAfAfauguuccacu	3927	PaGfugdGa(Agn)cauuucAfcCfgucaucu	5408	AGAUGACGGUGAAAUGUUCCACA	6889
AD-1948864	ugacggugAfAfAfuguuccacau	3928	PadTgudGgdAacaudTuCfaccgucauc	5409	GAUGACGGUGAAAUGUUCCACAC	6890
AD-1948865	ugacggUfgAfAfAfuguuccacau	3929	PaUfgudGg(Agn)acauuuCfaCfcgucauc	5410	GAUGACGGUGAAAUGUUCCACAC	6891
AD-1948866	gacggugaAfAfUfguuccacacu	3930	PadGugdTgdGaacadTuUfcaccgucau	5411	AUGACGGUGAAAUGUUCCACACA	6892
AD-1948867	acggugaaAfUfGfuuccacacau	3931	PadTgudGudGgaacdAuUfucaccguca	5412	UGACGGUGAAAUGUUCCACACAC	6893
AD-1948868	cggugaaaUfGfUfuccacacacu	3932	PadGugdTgdTggaadCaUfuucaccguc	5413	GACGGUGAAAUGUUCCACACACU	6894
AD-1948869	cggugaAfaUfGfUfuccacacacu	3933	PaGfugdTg(Tgn)ggaacaUfuUfcaccguc	5414	GACGGUGAAAUGUUCCACACACU	6895
AD-1948870	ggugaaauGfUfUfccacacacuu	3934	PadAgudGudGuggadAcAfuuucaccgu	5415	ACGGUGAAAUGUUCCACACACUG	6896
AD-1948871	gugaaaugUfUfCfcacacacugu	3935	PadCagdTgdTguggdAaCfauuucaccg	5416	CGGUGAAAUGUUCCACACACUGG	6897
AD-1948872	gugaaaUfgUfUfCfcacacacugu	3936	PaCfagdTg(Tgn)guggaaCfaUfuucaccg	5417	CGGUGAAAUGUUCCACACACUGG	6898
AD-1948873	gaaauguuCfCfAfcacuggau	3937	PadTccdAgdTgugudGgAfacauuucac	5418	GUGAAAUGUUCCACACACUGGAU	6899
AD-1948874	gaaaugUfuCfCfAfcacacuggau	3938	PaUfccdAg(Tgn)guguggAfaCfauuucac	5419	GUGAAAUGUUCCACACACUGGAU	6900
AD-1948875	aaauguucCfAfCfacacuggauu	3939	PadAucdCadGugugdTgGfaacauuuca	5420	UGAAAUGUUCCACACACUGGAUG	6901
AD-1948876	aauguuccAfCfAfcacuggaugu	3940	PadCaudCcdAgugudGuGfgaacauuuc	5421	GAAAUGUUCCACACACUGGAUGA	6902

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948877	auguuccaCfAfCfacuggaugau	3941	PadTcadTcdCagugdTgUfggaacauuu	5422	AAAUGUUCCACACACUGGAUGAU	6903
AD-1948878	uguuccacAfCfAfcuggaugauu	3942	PadAucdAudCcagudGuGfuggaacauu	5423	AAUGUUCCACACACUGGAUGAUG	6904
AD-1948879	guuccacaCfAfCfuggaugaugu	3943	PadCaudCadTccagdTgUfguggaacau	5424	AUGUUCCACACACUGGAUGAUGG	6905
AD-1948880	ccacacaaGfAfUfuuacagaucu	3944	PadGaudCudGuaaadTcUfugugguggcc	5425	GGCCACACAAGAUUUACAGAUCU	6906
AD-1948881	cacacaagAfUfUfuacagaucuu	3945	PadAgadTcdTguaadAuCfuuguguggc	5426	GCCACACAAGAUUUACAGAUCUA	6907
AD-1948882	cacacaAfgAfUfUfuacagaucuu	3946	PaAfgadTc(Tgn)guaaauCfuUfguguggc	5427	GCCACACAAGAUUUACAGAUCUA	6908
AD-1948883	acacaagaUfUfUfacagaucuau	3947	PadTagdAudCuguadAaUfcuugugugg	5428	CCACACAAGAUUUACAGAUCUAA	6909
AD-1948884	cacaagauUfUfAfcagaucuaau	3948	PadTuadGadTcugudAaAfucuugugug	5429	CACACAAGAUUUACAGAUCUAAU	6910
AD-1948885	cacaagAfuUfUfAfcagaucuaau	3949	PaUfuadGa(Tgn)cuguaaAfuCfuugugug	5430	CACACAAGAUUUACAGAUCUAAU	6911
AD-1948886	acaagauuUfAfCfagaucuaauu	3950	PadAuudAgdAucugdTaAfaucuugugu	5431	ACACAAGAUUUACAGAUCUAAUA	6912
AD-1948887	acaagaUfuUfAfCfagaucuaauu	3951	PaAfuudAg(Agn)ucuguaAfaUfcuugugu	5432	ACACAAGAUUUACAGAUCUAAUA	6913
AD-1948888	caagauuuAfCfAfgaucuaauau	3952	PadTaudTadGaucudGuAfaaucuugug	5433	CACAAGAUUUACAGAUCUAAUAC	6914
AD-1948889	aagauuuaCfAfGfaucuaauacu	3953	PadGuadTudAgaucdTgUfaaaucuugu	5434	ACAAGAUUUACAGAUCUAAUACA	6915
AD-1948890	aagauuUfaCfAfGfaucuaauacu	3954	PaGfuadTu(Agn)gaucugUfaAfaucuugu	5435	ACAAGAUUUACAGAUCUAAUACA	6916
AD-1948891	agauuuacAfGfAfucuaauacau	3955	PadTgudAudTagaudCuGfuaaaucuug	5436	CAAGAUUUACAGAUCUAAUACAG	6917
AD-1948892	agauuuAfcAfGfAfucuaauacau	3956	PaUfgudAu(Tgn)agaucuGfuAfaaucuug	5437	CAAGAUUUACAGAUCUAAUACAG	6918
AD-1948893	agcuggugGfAfGfucuaucaau	3957	PadTugdAudAgaacdTcCfaccagcugu	5438	ACAGCUGGUGGAGUUCUAUCAAC	6919
AD-1948894	agcuggUfgGfAfGfuucuaucaau	3958	PaUfugdAu(Agn)gaacucCfaCfcagcugu	5439	ACAGCUGGUGGAGUUCUAUCAAC	6920
AD-1948895	gcugguggAfGfUfucuaucaacu	3959	PadGuudGadTagaadCuCfcaccagcug	5440	CAGCUGGUGGAGUUCUAUCAACU	6921
AD-1948896	gcugguGfgAfGfUfucuaucaacu	3960	PaGfuudGa(Tgn)agaacuCfcAfccagcug	5441	CAGCUGGUGGAGUUCUAUCAACU	6922
AD-1948897	cugguggaGfUfUfcuaucaacuu	3961	PadAgudTgdAuagadAcUfccaccagcu	5442	AGCUGGUGGAGUUCUAUCAACUC	6923
AD-1948898	cuggugGfaGfUfUfcuaucaacuu	3962	PaAfgudTg(Agn)uagaacUfcCfaccagcu	5443	AGCUGGUGGAGUUCUAUCAACUC	6924
AD-1948899	ugguggagUfUfCfuaucaacucu	3963	PadGagdTudGauagdAaCfuccaccagc	5444	GCUGGUGGAGUUCUAUCAACUCA	6925
AD-1948900	gguggaguUfCfUfaucaacucau	3964	PadTgadGudTgauadGaAfcuccaccag	5445	CUGGUGGAGUUCUAUCAACUCAA	6926

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948901	gguggaGfuUfCfUfaucaacucau	3965	PaUfgadGu(Tgn)gauagaAfcUfccaccag	5446	CUGGUGGAGUUCUAUCAACUCAA	6927
AD-1948902	guggaguuCfUfAfucaacucaau	3966	PadTugdAgdTugaudAgAfacuccacca	5447	UGGUGGAGUUCUAUCAACUCAAU	6928
AD-1948903	guggagUfuCfUfAfucaacucaau	3967	PaUfugdAg(Tgn)ugauagAfaCfuccacca	5448	UGGUGGAGUUCUAUCAACUCAAU	6929
AD-1948904	uggaguucUfAfUfcaacucaauu	3968	PadAuudGadGuugadTaGfaacuccacc	5449	GGUGGAGUUCUAUCAACUCAAUA	6930
AD-1948905	ggaguucuAfUfCfaacucaauau	3969	PadTaudTgdAguugdAuAfgaacuccac	5450	GUGGAGUUCUAUCAACUCAAUAA	6931
AD-1948906	ggaguuCfuAfUfCfaacucaauau	3970	PaUfaudTg(Agn)guugauAfgAfacuccac	5451	GUGGAGUUCUAUCAACUCAAUAA	6932
AD-1948907	gaguucuaUfCfAfacucaauaau	3971	PadTuadTudGaguudGaUfagaacucca	5452	UGGAGUUCUAUCAACUCAAUAAG	6933
AD-1948908	aguucuauCfAfAfcucaauaagu	3972	PadCuudAudTgagudTgAfuagaacucc	5453	GGAGUUCUAUCAACUCAAUAAGG	6934
AD-1948909	guucuaucAfAfCfucaauaaggu	3973	PadCcudTadTugagdTuGfauagaacuc	5454	GAGUUCUAUCAACUCAAUAAGGG	6935
AD-1948910	uucuaucaAfCfUfcaauaagggu	3974	PadCccdTudAuugadGuUfgauagaacu	5455	AGUUCUAUCAACUCAAUAAGGGC	6936
AD-1948911	ucuaucaaCfUfCfaauaagggcu	3975	PadGccdCudTauugdAgUfugauagaac	5456	GUUCUAUCAACUCAAUAAGGGCG	6937
AD-1948912	uaucaacuCfAfAfuaagggcguu	3976	PadAcgdCcdCuuaudTgAfguugauaga	5457	UCUAUCAACUCAAUAAGGGCGUU	6938
AD-1948913	aucaacucAfAfUfaagggcguuu	3977	PadAacdGcdCcuuadTuGfaguugauag	5458	CUAUCAACUCAAUAAGGGCGUUC	6939
AD-1948914	ucaacucaAfUfAfagggcguucu	3978	PadGaadCgdCccuudAuUfgaguugaua	5459	UAUCAACUCAAUAAGGGCGUUCU	6940
AD-1948915	caacucaaUfAfAfgggcguucuu	3979	PadAgadAcdGcccudTaUfugaguugau	5460	AUCAACUCAAUAAGGGCGUUCUU	6941
AD-1948916	aacucaauAfAfGfggcguucuuu	3980	PadAagdAadCgcccdTuAfuugaguuga	5461	UCAACUCAAUAAGGGCGUUCUUC	6942
AD-1948917	acucaauaAfGfGfgcguucuucu	3981	PadGaadGadAcgccdCuUfauugaguug	5462	CAACUCAAUAAGGGCGUUCUUCC	6943
AD-1948918	acucaaUfaAfGfGfgcguucuucu	3982	PaGfaadGa(Agn)cgcccuUfaUfugaguug	5463	CAACUCAAUAAGGGCGUUCUUCC	6944
AD-1948919	cucaauaaGfGfGfcguucuuccu	3983	PadGgadAgdAacgcdCcUfuauugaguu	5464	AACUCAAUAAGGGCGUUCUUCCU	6945
AD-1948920	ucaauaagGfGfCfguucuuccuu	3984	PadAggdAadGaacgdCcCfuuauugagu	5465	ACUCAAUAAGGGCGUUCUUCCUU	6946
AD-1948921	caauaaggGfCfGfucuuccuuu	3985	PadAagdGadAgaacdGcCfcuuauugag	5466	CUCAAUAAGGGCGUUCUUCCUUG	6947
AD-1948922	caauaaGfgGfCfGfuucuuccuuu	3986	PaAfagdGa(Agn)gaacgcCfcUfuauugag	5467	CUCAAUAAGGGCGUUCUUCCUUG	6948
AD-1948923	aauaagggCfGfUfucuuccuugu	3987	PadCaadGgdAagaadCgCfccuuauuga	5468	UCAAUAAGGGCGUUCUUCCUUGC	6949
AD-1948924	aagggcguUfCfUfuccuugcaau	3988	PadTugdCadAggaadGaAfcgcccuuau	5469	AUAAGGGCGUUCUUCCUUGCAAG	6950

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948925	aagggcGfuUfCfUfuccuugcaau	3989	PaUfugdCa(Agn)ggaagaAfcGfcccuuau	5470	AUAAGGGCGUUCUUCCUUGCAAG	6951
AD-1948926	ggcguucuUfCfCfuugcaaguuu	3990	PadAacdTudGcaagdGaAfgaacgcccu	5471	AGGGCGUUCUUCCUUGCAAGUUG	6952
AD-1948927	gcguucuuCfCfUfugcaaguugu	3991	PadCaadCudTgcaadGgAfagaacgccc	5472	GGGCGUUCUUCCUUGCAAGUUGA	6953
AD-1948928	cguucuucCfUfUfgcaaguugau	3992	PadTcadAcdTugcadAgGfaagaacgcc	5473	GGCGUUCUUCCUUGCAAGUUGAA	6954
AD-1948929	cguucuUfcCfUfUfgcaaguugau	3993	PaUfcadAc(Tgn)ugcaagGfaAfgaacgcc	5474	GGCGUUCUUCCUUGCAAGUUGAA	6955
AD-1948930	guucuuccUfUfGfcaaguugaau	3994	PadTucdAadCuugcdAaGfgaagaacgc	5475	GCGUUCUUCCUUGCAAGUUGAAA	6956
AD-1948931	uucuuccuUfGfCfaaguugaaau	3995	PadTuudCadAcuugdCaAfggaagaacg	5476	CGUUCUUCCUUGCAAGUUGAAAC	6957
AD-1948932	uucuucCfuUfGfCfaaguugaaau	3996	PaUfuudCa(Agn)cuugcaAfgGfaagaacg	5477	CGUUCUUCCUUGCAAGUUGAAAC	6958
AD-1948933	ucuuccuuGfCfAfaguugaaacu	3997	PadGuudTcdAacuudGcAfaggaagaac	5478	GUUCUUCCUUGCAAGUUGAAACA	6959
AD-1948934	ucuuccUfuGfCfAfaguugaaacu	3998	PaGfuudTc(Agn)acuugcAfaGfgaagaac	5479	GUUCUUCCUUGCAAGUUGAAACA	6960
AD-1948935	cuuccuugCfAfAfguugaaacau	3999	PadTgudTudCaacudTgCfaaggaagaa	5480	UUCUUCCUUGCAAGUUGAAACAU	6961
AD-1948936	uuccuugcAfAfGfuugaaacauu	4000	PadAugdTudTcaacdTuGfcaaggaaga	5481	UCUUCCUUGCAAGUUGAAACAUU	6962
AD-1948937	uuccuuGfcAfAfGfuugaaacauu	4001	PaAfugdTu(Tgn)caacuuGfcAfaggaaga	5482	UCUUCCUUGCAAGUUGAAACAUU	6963
AD-1948938	uccuugcaAfGfUfugaaacauuu	4002	PadAaudGudTucaadCuUfgcaaggaag	5483	CUUCCUUGCAAGUUGAAACAUUA	6964
AD-1948939	uccuugCfaAfGfUfugaaacauuu	4003	PaAfaudGu(Tgn)ucaacuUfgCfaaggaag	5484	CUUCCUUGCAAGUUGAAACAUUA	6965
AD-1948940	ccuugcaaGfUfUfgaaacauuau	4004	PadTaadTgdTuucadAcUfugcaaggaa	5485	UUCCUUGCAAGUUGAAACAUUAU	6966
AD-1948941	ccuugcAfaGfUfUfgaaacauuau	4005	PaUfaadTg(Tgn)uucaacUfuGfcaaggaa	5486	UUCCUUGCAAGUUGAAACAUUAU	6967
AD-1948942	cuugcaagUfUfGfaaacauuauu	4006	PadAuadAudGuuucdAaCfuugcaagga	5487	UCCUUGCAAGUUGAAACAUUAUU	6968
AD-1948943	uugcaaguUfGfAfacauuauuu	4007	PadAaudAadTguuudCaAfcuugcaagg	5488	CCUUGCAAGUUGAAACAUUAUUG	6969
AD-1948944	ugcaaguuGfAfAfacauuauugu	4008	PadCaadTadAuguudTcAfacuugcaag	5489	CUUGCAAGUUGAAACAUUAUUGU	6970
AD-1948945	gcaaguugAfAfAfcauuauuguu	4009	PadAcadAudAaugudTuCfaacuugcaa	5490	UUGCAAGUUGAAACAUUAUUGUG	6971
AD-1948946	caaguugaAfAfCfauuauugugu	4010	PadCacdAadTaaugdTuUfcaacuugca	5491	UGCAAGUUGAAACAUUAUUGUGC	6972
AD-1948947	aaguugaaAfCfAfuuauugugcu	4011	PadGcadCadAuaaudGuUfucaacuugc	5492	GCAAGUUGAAACAUUAUUGUGCU	6973
AD-1948948	aguugaaaCfAfUfuauugugcuu	4012	PadAgcdAcdAauaadTgUfuucaacuug	5493	CAAGUUGAAACAUUAUUGUGCUA	6974

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948949	guugaaacAfUfUfa uugugcuau	4013	PadTagdCadCaauadAu Gfuuucaacuu	5494	AAGUUGAAACAUU AUUGUGCUAG	6975
AD-1948950	uugaaacaUfUfAfu ugugcuagu	4014	PadCuadGcdAcaaudA aUfguuucaacu	5495	AGUUGAAACAUUA UUGUGCUAGG	6976
AD-1948951	uugaaaCfaUfUfAf uugugcuagu	4015	PaCfuadGc(Agn)caaua aUfgUfuucaacu	5496	AGUUGAAACAUUA UUGUGCUAGG	6977
AD-1948952	ugaaacauUfAfUfu gugcuaggu	4016	PadCcudAgdCacaadTa Afuguuucaac	5497	GUUGAAACAUUAU UGUGCUAGGA	6978
AD-1948953	aaacauuaUfUfGfu gcuaggauu	4017	PadAucdCudAgcacdA aUfaauguuuca	5498	UGAAACAUUAUUG UGCUAGGAUU	6979
AD-1948954	aaacauUfaUfUfGf ugcuaggauu	4018	PaAfucdCu(Agn)gcaca aUfaAfuguuuca	5499	UGAAACAUUAUUG UGCUAGGAUU	6980
AD-1948955	aacauuauUfGfUfg cuaggauuu	4019	PadAaudCcdTagcadCa Afuaauguuuc	5500	GAAACAUUAUUGU GCUAGGAUUG	6981
AD-1948956	aacauuAfuUfGfUf gcuaggauuu	4020	PaAfaudCc(Tgn)agcac aAfuAfauguuuc	5501	GAAACAUUAUUGU GCUAGGAUUG	6982
AD-1948957	acauuauuGfUfGfc uaggauugu	4021	PadCaadTcdCuagcdAc Afauaauguuu	5502	AAACAUUAUUGUG CUAGGAUUGC	6983
AD-1948958	cauuauugUfGfCfu aggauugcu	4022	PadGcadAudCcuagdC aCfaauaauguu	5503	AACAUUAUUGUGC UAGGAUUGCU	6984
AD-1948959	auuauuguGfCfUfa ggauugcuu	4023	PadAgcdAadTccuadGc Afcaauaaugu	5504	ACAUUAUUGUGCU AGGAUUGCUC	6985
AD-1948960	uuauugugCfUfAfg gauugcucu	4024	PadGagdCadAuccudA gCfacaauaaug	5505	CAUUAUUGUGCUA GGAUUGCUCU	6986
AD-1948961	uuauugUfgCfUfAf ggauugcucu	4025	PaGfagdCa(Agn)uccua gCfaCfaauaaug	5506	CAUUAUUGUGCUA GGAUUGCUCU	6987
AD-1948962	uauugugcUfAfGfg auugcucuu	4026	PadAgadGcdAauccdTa Gfcacaauaau	5507	AUUAUUGUGCUAG GAUUGCUCUC	6988
AD-1948963	uauuguGfcUfAfGf gauugcucuu	4027	PaAfgadGc(Agn)auccu aGfcAfcaauaau	5508	AUUAUUGUGCUAG GAUUGCUCUC	6989
AD-1948964	auugugcuAfGfGfa uugcucucu	4028	PadGagdAgdCaaucdC uAfgcacaauaa	5509	UUAUUGUGCUAGG AUUGCUCUCU	6990
AD-1948965	uugugcuaGfGfAfu ugcucucuu	4029	PadAgadGadGcaaudC cUfagcacaaua	5510	UAUUGUGCUAGGA UUGCUCUCUA	6991
AD-1948966	ugugcuagGfAfUfu gcucucuau	4030	PadTagdAgdAgcaadTc Cfuagcacaau	5511	AUUGUGCUAGGAU UGCUCUCUAG	6992
AD-1948967	ugugcuAfgGfAfUf ugcucucuau	4031	PaUfagdAg(Agn)gcaau cCfuAfgcacaau	5512	AUUGUGCUAGGAU UGCUCUCUAG	6993
AD-1948968	gugcuaggAfUfUfg cucucuagu	4032	PadCuadGadGagcadA uCfcuagcacaa	5513	UUGUGCUAGGAUU GCUCUCUAGA	6994
AD-1948969	agccagaaGfUfGfac uuauuaau	4033	PadTuadAudAagucdA cUfucuggcuug	5514	CAAGCCAGAAGUG ACUUAUUAAA	6995
AD-1948970	gccagaagUfGfAfc uuauuaaau	4034	PadTuudAadTaagudCa Cfuucuggcuu	5515	AAGCCAGAAGUGA CUUAUUAAAC	6996
AD-1948971	ccagaaguGfAfCfu uauuaaacu	4035	PadGuudTadAuaagdTc Afcuucuggcu	5516	AGCCAGAAGUGAC UUAUUAAACU	6997
AD-1948972	cagaagugAfCfUfu auuaaacuu	4036	PadAgudTudAauaadG uCfacuucuggc	5517	GCCAGAAGUGACU UAUUAAACUA	6998

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948973	agaagugaCfUfUfauuaaacuau	4037	PadTagdTudTaauadAgUfcacuucugg	5518	CCAGAAGUGACUUAUUAAACUAU	6999
AD-1948974	agaaguGfaCfUfUfauuaaacuau	4038	PaUfagdTu(Tgn)aauaagUfcAfcuucugg	5519	CCAGAAGUGACUUAUUAAACUAU	7000
AD-1948975	gaagugacUfUfAfuuaaacuauu	4039	PadAuadGudTuaaudAaGfucacuucug	5520	CAGAAGUGACUUAUUAAACUAUU	7001
AD-1948976	gaagugAfcUfUfAfuuaaacuauu	4040	PaAfuadGu(Tgn)uaauaaGfuCfacuucug	5521	CAGAAGUGACUUAUUAAACUAUU	7002
AD-1948977	aagugacuUfAfUfuaaacuauuu	4041	PadAaudAgdTuuaadTaAfgucacuucu	5522	AGAAGUGACUUAUUAAACUAUUG	7003
AD-1948978	aagugaCfuUfAfUfuaaacuauuu	4042	PaAfaudAg(Tgn)uuaauaAfgUfcacuucu	5523	AGAAGUGACUUAUUAAACUAUUG	7004
AD-1948979	agugacuuAfUfUfaaacuauugu	4043	PadCaadTadGuuuadAuAfagucacuuc	5524	GAAGUGACUUAUUAAACUAUUGA	7005
AD-1948980	ugacuuauUfAfAfacuauugaau	4044	PadTucdAadTaguudTaAfuaagucacu	5525	AGUGACUUAUUAAACUAUUGAAG	7006
AD-1948981	gacuuauuAfAfAfcuauugaagu	4045	PadCuudCadAuagudTuAfauaagucac	5526	GUGACUUAUUAAACUAUUGAAGG	7007
AD-1948982	ggaaaaggAfCfUfcaagaaaaau	4046	PadTuudTudCuugadGuCfcuuuuccuu	5527	AAGGAAAAGGACUCAAGAAAAAU	7008
AD-1948983	gaaaaggaCfUfCfaagaaaaauu	4047	PadAuudTudTcuugdAgUfccuuuuccu	5528	AGGAAAAGGACUCAAGAAAAAUA	7009
AD-1948984	gaaaagGfaCfUfCfaagaaaaauu	4048	PaAfuudTu(Tgn)cuugagUfcCfuuuuccu	5529	AGGAAAAGGACUCAAGAAAAAUA	7010
AD-1948985	aaaaggacUfCfAfagaaaaauau	4049	PadTaudTudTucuudGaGfuccuuuucc	5530	GGAAAAGGACUCAAGAAAAAUAA	7011
AD-1948986	aaaaggAfcUfCfAfagaaaaauau	4050	PaUfaudTu(Tgn)ucuugaGfuCfcuuuucc	5531	GGAAAAGGACUCAAGAAAAAUAA	7012
AD-1948987	aaaggacuCfAfAfgaaaaauau	4051	PadTuadTudTuucudTgAfguccuuuuc	5532	GAAAAGGACUCAAGAAAAAUAAU	7013
AD-1948988	aaaggaCfuCfAfAfgaaaaauau	4052	PaUfuadTu(Tgn)uucuugAfgUfccuuuuc	5533	GAAAAGGACUCAAGAAAAAUAAU	7014
AD-1948989	acucaagaAfAfAfauaauaaau	4053	PadTuudTadTuauudTuUfcuugagucc	5534	GGACUCAAGAAAAAUAAUAAAAG	7015
AD-1948990	acucaaGfaAfAfAfauaauaaaau	4054	PaUfuudTa(Tgn)uauuuuUfcUfugagucc	5535	GGACUCAAGAAAAAUAAUAAAAG	7016
AD-1948991	caagaaaaAfUfAfauaaaagacu	4055	PadGucdTudTuauudAuUfuuucuugag	5536	CUCAAGAAAAAUAAUAAAAGACC	7017
AD-1948992	caagaaAfaAfUfAfauaaaagacu	4056	PaGfucdTu(Tgn)uauuauUfuUfucuugag	5537	CUCAAGAAAAAUAAUAAAAGACC	7018
AD-1948993	auaaaagaCfCfAfuaaauaaggu	4057	PadCcudTadTuuaudGgUfcuuuuauua	5538	UAAUAAAAGACCAUAAAUAAGGG	7019
AD-1948994	uaaaagacCfAfUfaaauaagggu	4058	PadCccdTudAuuuadTgGfucuuuuauu	5539	AAUAAAAGACCAUAAAUAAGGGC	7020
AD-1948995	accaugugAfAfAfagaauguauu	4059	PadAuadCadTucuudTuCfacaugguaa	5540	UUACCAUGUGAAAAGAAUGUAUU	7021
AD-1948996	ccaugugaAfAfAfgaauguauuu	4060	PadAaudAcdAuucudTuUfcacauggua	5541	UACCAUGUGAAAAGAAUGUAUUU	7022

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1948997	ccauguGfaAfAfAfAfgaauguauuu	4061	PaAfaudAc(Agn)uucuuuUfcAfcauggua	5542	UACCAUGUGAAAAGAAUGUAUUU	7023
AD-1948998	caugugaaAfAfGfaauguauuuu	4062	PadAaadTadCauucdTuUfucacauggu	5543	ACCAUGUGAAAAGAAUGUAUUUC	7024
AD-1948999	ucaccugcAfAfGfuuacaaaaau	4063	PadTuudTudGuaacdTuGfcaggugaaa	5544	UUUCACCUGCAAGUUACAAAAAA	7025
AD-1949000	caccugcaAfGfUfuacaaaaaau	4064	PadTuudTudTguaadCuUfgcaggugaa	5545	UUCACCUGCAAGUUACAAAAAAA	7026
AD-1949001	caccugCfaAfGfUfuacaaaaaau	4065	PaUfuudTu(Tgn)guaacuUfgCfaggugaa	5546	UUCACCUGCAAGUUACAAAAAAA	7027
AD-1949002	accugcaaGfUfUfacaaaaaaau	4066	PadTuudTudTuguadAcUfugcagguga	5547	UCACCUGCAAGUUACAAAAAAAU	7028
AD-1949003	accugcAfaGfUfUfacaaaaaaau	4067	PaUfuudTu(Tgn)uguaacUfuGfcagguga	5548	UCACCUGCAAGUUACAAAAAAAU	7029
AD-1949004	aaaaaaauAfGfUfuugugcauuu	4068	PadAaudGcdAcaaadCuAfuuuuuuuugu	5549	ACAAAAAAAUAGUUUGUGCAUUG	7030
AD-1949005	aaaaaaAfuAfGfUfuugugcauuu	4069	PaAfaudGc(Agn)caaacuAfuUfuuuuugu	5550	ACAAAAAAAUAGUUUGUGCAUUG	7031
AD-1949006	ugcaaauaAfGfCfaaagacuugu	4070	PadCaadGudCuuugdCuUfauuugcaau	5551	AUUGCAAAUAAGCAAAGACUUGG	7032
AD-1949007	gcaaauaaGfCfAfaagacuuggu	4071	PadCcadAgdTcuuudGcUfuauuugcaa	5552	UUGCAAAUAAGCAAAGACUUGGA	7033
AD-1949008	caaauaagCfAfAfagacuuggau	4072	PadTccdAadGucuudTgCfuuauuugca	5553	UGCAAAUAAGCAAAGACUUGGAU	7034
AD-1949009	aaauaagcAfAfAfgacuuggauu	4073	PadAucdCadAgucudTuGfcuuauuugc	5554	GCAAAUAAGCAAAGACUUGGAUU	7035
AD-1949010	aaauaaGfcAfAfAfgacuuggauu	4074	PaAfucdCa(Agn)gucuuuGfcUfuauuugc	5555	GCAAAUAAGCAAAGACUUGGAUU	7036
AD-1949011	aauaagcaAfAfGfacuuggauuu	4075	PadAaudCcdAagucdTuUfgcuuauuug	5556	CAAAUAAGCAAAGACUUGGAUUG	7037
AD-1949012	auaagcaaAfGfAfcuuggauugu	4076	PadCaadTcdCaagudCuUfugcuuauuu	5557	AAAUAAGCAAAGACUUGGAUUGA	7038
AD-1949013	uaagcaaaGfAfCfuuggauugau	4077	PadTcadAudCcaagdTcUfuugcuuauu	5558	AAUAAGCAAAGACUUGGAUUGAC	7039
AD-1949014	aagcaaagAfCfUfuggauugacu	4078	PadGucdAadTccaadGuCfuuugcuuau	5559	AUAAGCAAAGACUUGGAUUGACU	7040
AD-1949015	aagcaaAfgAfCfUfuggauugacu	4079	PaGfucdAa(Tgn)ccaaguCfuUfugcuuau	5560	AUAAGCAAAGACUUGGAUUGACU	7041
AD-1949016	agcaaagaCfUfUfggauugacuu	4080	PadAgudCadAuccadAgUfcuuugcuua	5561	UAAGCAAAGACUUGGAUUGACUU	7042
AD-1949017	agcaaaGfaCfUfUfggauugacuu	4081	PaAfgudCa(Agn)uccaagUfcUfuugcuua	5562	UAAGCAAAGACUUGGAUUGACUU	7043
AD-1949018	gcaaagacUfUfGfgauugacuuu	4082	PadAagdTcdAauccdAaGfucuuugcuu	5563	AAGCAAAGACUUGGAUUGACUUU	7044
AD-1949019	gcaaagAfcUfUfGfgauugacuuu	4083	PaAfagdTc(Agn)auccaaGfuCfuuugcuu	5564	AAGCAAAGACUUGGAUUGACUUU	7045
AD-1949020	caaagacuUfGfGfauugacuuuu	4084	PadAaadGudCaaucdCaAfgucuuugcu	5565	AGCAAAGACUUGGAUUGACUUUA	7046

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-1949021	aaagacuuGfGfAfuugacuuuau	4085	PadTaadAgdTcaaudCcAfagucuuugc	5566	GCAAAGACUUGGAUUGACUUUAC	7047
AD-1949022	aaagacUfuGfGfAfuugacuuuau	4086	PaUfaadAg(Tgn)caauccAfaGfucuuugc	5567	GCAAAGACUUGGAUUGACUUUAC	7048
AD-1949023	aagacuugGfAfUfugacuuuacu	4087	PadGuadAadGucaadTcCfaagucuuug	5568	CAAAGACUUGGAUUGACUUUACA	7049
AD-1949024	agacuuggAfUfUfgacuuuacau	4088	PadTgudAadAgucadAuCfcaagucuuu	5569	AAAGACUUGGAUUGACUUUACAU	7050
AD-1949025	agacuuGfgAfUfUfgacuuuacau	4089	PaUfgudAa(Agn)gucaauCfcAfagucuuu	5570	AAAGACUUGGAUUGACUUUACAU	7051
AD-1949026	gacuuggaUfUfGfacuuuacauu	4090	PadAugdTadAagucdAaUfccaagucuu	5571	AAGACUUGGAUUGACUUUACAUU	7052
AD-1949027	acuuggauUfGfAfcuuuacauuu	4091	PadAaudGudAaagudCaAfuccaagucu	5572	AGACUUGGAUUGACUUUACAUUC	7053
AD-1949028	cuuggauuGfAfCfuuuacauucu	4092	PadGaadTgdTaaagdTcAfauccaaguc	5573	GACUUGGAUUGACUUUACAUUCA	7054
AD-1949029	cuuggaUfuGfAfCfuuuacauucu	4093	PaGfaadTg(Tgn)aaagucAfaUfccaaguc	5574	GACUUGGAUUGACUUUACAUUCA	7055
AD-1949030	uuggauugAfCfUfuuacauucau	4094	PadTgadAudGuaaadGuCfaauccaagu	5575	ACUUGGAUUGACUUUACAUUCAU	7056
AD-1949031	uggauugaCfUfUfuacauucauu	4095	PadAugdAadTguaadAgUfcaauccaag	5576	CUUGGAUUGACUUUACAUUCAUC	7057
AD-1949032	ggauugacUfUfUfacauucaucu	4096	PadGaudGadAuguadAaGfucaauccaa	5577	UUGGAUUGACUUUACAUUCAUCA	7058
AD-1949033	ggauugAfcUfUfUfacauucaucu	4097	PaGfaudGa(Agn)uguaaaGfuCfaauccaa	5578	UUGGAUUGACUUUACAUUCAUCA	7059
AD-1949034	gauugacuUfUfAfcauucaucau	4098	PadTgadTgdAaugudAaAfgucaaucca	5579	UGGAUUGACUUUACAUUCAUCAU	7060
AD-1949035	gauugaCfuUfUfAfcauucaucau	4099	PaUfgadTg(Agn)auguaaAfgUfcaaucca	5580	UGGAUUGACUUUACAUUCAUCAU	7061
AD-1949036	auugacuuUfAfCfauucaucauu	4100	PadAugdAudGaaugdTaAfagucaaucc	5581	GGAUUGACUUUACAUUCAUCAUU	7062
AD-1949037	uugacuuuAfCfAfucaucauuu	4101	PadAaudGadTgaaudGuAfaagucaauc	5582	GAUUGACUUUACAUUCAUCAUUU	7063
AD-1949038	uugacuUfuAfCfAfuucaucauuu	4102	PaAfaudGa(Tgn)gaaguaAfaAfgucaauc	5583	GAUUGACUUUACAUUCAUCAUUU	7064
AD-2017365.1	guguugucAfGfCfagaccuauuu	4103	PadAaudAgdGucugdCuGfacaacacag	5584	CUGUGUUGUCAGCAGACCUAUUU	7065
AD-2017366.1	uguugucaGfCfAfgaccuauuuu	4104	PadAaadTadGgucudGcUfgacaacaca	5585	UGUGUUGUCAGCAGACCUAUUUC	7066
AD-2017367.1	guugucagCfAfGfaccuauuucu	4105	PadGaadAudAggucdTgCfugacaacac	5586	GUGUUGUCAGCAGACCUAUUUCC	7067
AD-2017368.1	uugucagcAfGfAfccuauuuccu	4106	PadGgadAadTaggudCuGfcugacaaca	5587	UGUUGUCAGCAGACCUAUUUCCC	7068
AD-2017369.1	ugucagcaGfAfCfcuauuucccu	4107	PadGggdAadAuaggdTcUfgcugacaac	5588	GUUGUCAGCAGACCUAUUUCCCA	7069
AD-2017370.1	gucagcagAfCfCfuauuucccau	4108	PadTggdGadAauagdGuCfugcugacaa	5589	UUGUCAGCAGACCUAUUUCCCAA	7070

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017371.1	ucagcagaCfCfUfauuucccaau	4109	PadTugdGgdAaauadGgUfcugcugaca	5590	UGUCAGCAGACCUAUUUCCCAAA	7071
AD-2017372.1	cagcagacCfUfAfuuucccaaau	4110	PadTuudGgdGaaaudAgGfucugcugac	5591	GUCAGCAGACCUAUUUCCCAAAG	7072
AD-2017373.1	agcagaccUfAfUfuucccaaagu	4111	PadCuudTgdGgaaadTaGfgucugcuga	5592	UCAGCAGACCUAUUUCCCAAAGC	7073
AD-2017374.1	gcagaccuAfUfUfucccaaagcu	4112	PadGcudTudGggaadAuAfggucugcug	5593	CAGCAGACCUAUUUCCCAAAGCA	7074
AD-2017375.1	cagaccuaUfUfUfccaaagcau	4113	PadTgcdTudTgggadAaUfaggucugcu	5594	AGCAGACCUAUUUCCCAAAGCAA	7075
AD-2017376.1	agaccuauUfUfCfccaaagcaau	4114	PadTugdCudTugggdAaAfuaggucugc	5595	GCAGACCUAUUUCCCAAAGCAAA	7076
AD-2017377.1	gaccuauuUfCfCfcaaagcaaau	4115	PadTuudGcdTuuggdGaAfauaggucug	5596	CAGACCUAUUUCCCAAAGCAAAU	7077
AD-2017378.1	accuauuuCfCfCfaaagcaaauu	4116	PadAuudTgdCuuugdGgAfaauaggucu	5597	AGACCUAUUUCCCAAAGCAAAUU	7078
AD-2017379.1	ccuauuucCfCfAfaagcaaauuu	4117	PadAaudTudGcuuudGgGfaaauagguc	5598	GACCUAUUUCCCAAAGCAAAUUC	7079
AD-2017380.1	cuauuuccCfAfAfagcaaauucu	4118	PadGaadTudTgcuudTgGfgaaauaggu	5599	ACCUAUUUCCCAAAGCAAAUUCA	7080
AD-2017381.1	aaaaacagGfUfGfauuaaaguau	4119	PadTacdTudTaaucdAcCfuguuuuuuc	5600	GAAAAAACAGGUGAUUAAAGUAU	7081
AD-2017382.1	aaacagguGfAfUfuaaaguauau	4120	PadTaudAcdTuuaadTcAfccuguuuuu	5601	AAAAACAGGUGAUUAAAGUAUAC	7082
AD-2017383.1	aacaggugAfUfUfaaaguauacu	4121	PadGuadTadCuuuadAuCfaccuguuuu	5602	AAAACAGGUGAUUAAAGUAUACA	7083
AD-2017384.1	acaggugaUfUfAfaaguauacau	4122	PadTgudAudAcuuudAaUfcaccuguuu	5603	AAACAGGUGAUUAAAGUAUACAG	7084
AD-2017385.1	caggugauUfAfAfaguauacagu	4123	PadCugdTadTacuudTaAfucaccuguu	5604	AACAGGUGAUUAAAGUAUACAGU	7085
AD-2017386.1	aggugauuAfAfAfguauacaguu	4124	PadAcudGudAuacudTuAfaucaccugu	5605	ACAGGUGAUUAAAGUAUACAGUG	7086
AD-2017387.1	ggugauuaAfAfGfuauacagugu	4125	PadCacdTgdTauacdTuUfaaucaccug	5606	CAGGUGAUUAAAGUAUACAGUGA	7087
AD-2017388.1	gugauuaaAfGfUfauacagugau	4126	PadTcadCudGuauadCuUfuaaucaccu	5607	AGGUGAUUAAAGUAUACAGUGAA	7088
AD-2017389.1	ugauuaaaGfUfAfuacagugaau	4127	PadTucdAcdTguaudAcUfuuaaucacc	5608	GGUGAUUAAAGUAUACAGUGAAG	7089
AD-2017390.1	gauuaaagUfAfUfacagugaagu	4128	PadCuudCadCuguadTaCfuuuaaucac	5609	GUGAUUAAAGUAUACAGUGAAGA	7090
AD-2017391.1	auuaaaguAfUfAfcagugaagau	4129	PadTcudTcdAcugudAuAfcuuuaauca	5610	UGAUUAAAGUAUACAGUGAAGAU	7091
AD-2017392.1	uuaaaguaUfAfCfagugaagauu	4130	PadAucdTudCacugdTaUfacuuuaauc	5611	GAUUAAAGUAUACAGUGAAGAUG	7092
AD-2017393.1	uaaaguauAfCfAfgugaagaugu	4131	PadCaudCudTcacudGuAfuacuuuaau	5612	AUUAAAGUAUACAGUGAAGAUGA	7093
AD-2017394.1	aaaguauaCfAfGfugaagaugau	4132	PadTcadTcdTucacdTgUfauacuuuaa	5613	UUAAAGUAUACAGUGAAGAUGAA	7094

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017395.1	aaguauacAfGfUfg aagaugaau	4133	PadTucdAudCuucadC uGfuauacuuua	5614	UAAAGUAUACAGU GAAGAUGAAA	7095
AD-2017396.1	aguauacaGfUfGfaa gaugaaau	4134	PadTuudCadTcuucdAc Ufguauacuuu	5615	AAAGUAUACAGUG AAGAUGAAAC	7096
AD-2017397.1	guauacagUfGfAfa gaugaaacu	4135	PadGuudTcdAucuudC aCfuguauacuu	5616	AAGUAUACAGUGA AGAUGAAACC	7097
AD-2017398.1	acagugaaGfAfUfg aaaccagcu	4136	PadGcudGgdTuucadTc Ufucacuguau	5617	AUACAGUGAAGAU GAAACCAGCA	7098
AD-2017399.1	cagugaagAfUfGfa aaccagcau	4137	PadTgcdTgdGuuucdA uCfuucacugua	5618	UACAGUGAAGAUG AAACCAGCAG	7099
AD-2017400.1	agugaagaUfGfAfa accagcagu	4138	PadCugdCudGguuudC aUfcuucacugu	5619	ACAGUGAAGAUGA AACCAGCAGG	7100
AD-2017401.1	gugaagauGfAfAfa ccagcaggu	4139	PadCcudGcdTgguudTc Afucuucacug	5620	CAGUGAAGAUGAA ACCAGCAGGG	7101
AD-2017402.1	ugaagaugAfAfAfc cagcagggu	4140	PadCccdTgdCuggudTu Cfaucuucacu	5621	AGUGAAGAUGAAA CCAGCAGGGC	7102
AD-2017403.1	gaagaugaAfAfCfca gcagggcu	4141	PadGccdCudGcuggdT uUfcaucuucac	5622	GUGAAGAUGAAAC CAGCAGGGCU	7103
AD-2017404.1	aagaugaaAfCfCfag cagggcuu	4142	PadAgcdCcdTgcugdG uUfucaucuuca	5623	UGAAGAUGAAACC AGCAGGGCUU	7104
AD-2017405.1	agaugaaaCfCfAfgc agggcuuu	4143	PadAagdCcdCugcudG gUfuucaucuuc	5624	GAAGAUGAAACCA GCAGGGCUUU	7105
AD-2017406.1	gaugaaacCfAfGfca gggcuuuu	4144	PadAaadGcdCcugcdTg Gfuuucaucuu	5625	AAGAUGAAACCAG CAGGGCUUUA	7106
AD-2017407.1	augaaaccAfGfCfag ggcuuuau	4145	PadTaadAgdCccugdCu Gfguuucaucu	5626	AGAUGAAACCAGC AGGGCUUUAG	7107
AD-2017408.1	ugaaaccaGfCfAfgg gcuuuagu	4146	PadCuadAadGcccudG cUfgguuucauc	5627	GAUGAAACCAGCA GGGCUUUAGA	7108
AD-2017409.1	gaaaccagCfAfGfgg cuuuagau	4147	PadTcudAadAgcccdTg Cfugguuucau	5628	AUGAAACCAGCAG GGCUUUAGAU	7109
AD-2017410.1	aaaccagcAfGfGfgc uuuagauu	4148	PadAucdTadAagccdCu Gfcugguuuca	5629	UGAAACCAGCAGG GCUUUAGAUG	7110
AD-2017411.1	aaccagcaGfGfGfcu uuagaugu	4149	PadCaudCudAaagcdCc Ufgcugguuuc	5630	GAAACCAGCAGGG CUUUAGAUGU	7111
AD-2017412.1	accagcagGfGfCfuu uagauguu	4150	PadAcadTcdTaaagdCc Cfugcugguuu	5631	AAACCAGCAGGGC UUUAGAUGUA	7112
AD-2017413.1	ccagcaggGfCfUfu uagauguau	4151	PadTacdAudCuaaadGc Cfcugcugguu	5632	AACCAGCAGGGCU UUAGAUGUAC	7113
AD-2017414.1	cagcagggCfUfUfu agauguacu	4152	PadGuadCadTcuaadAg Cfccugcuggu	5633	ACCAGCAGGGCUU UAGAUGUACC	7114
AD-2017415.1	agcagggcUfUfUfa gauguaccu	4153	PadGgudAcdAucuadA aGfcccugcugg	5634	CCAGCAGGGCUUU AGAUGUACCC	7115
AD-2017416.1	aaagaacaAfUfAfga agaccacu	4154	PadGugdGudCuucudA uUfguucuuucu	5635	AGAAAGAACAAUA GAAGACCACG	7116
AD-2017417.1	aagaacaaUfAfGfaa gaccacgu	4155	PadCgudGgdTcuucdTa Ufuguucuuuc	5636	GAAAGAACAAUAG AAGACCACGA	7117
AD-2017418.1	agaacaauAfGfAfag accacgau	4156	PadTcgdTgdGucuudC uAfuuguucuuu	5637	AAAGAACAAUAGA AGACCACGAA	7118

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017419.1	gaacaauaGfAfAfgaccacgaau	4157	PadTucdGudGgucudTcUfauuguucuu	5638	AAGAACAAUAGAAGACCACGAAC	7119
AD-2017420.1	aacaauagAfAfGfaccacgaacu	4158	PadGuudCgdTggucdTuCfuauuguucu	5639	AGAACAAUAGAAGACCACGAACU	7120
AD-2017421.1	acaauagaAfGfAfccacgaacuu	4159	PadAgudTcdGuggudCuUfcuauuguuc	5640	GAACAAUAGAAGACCACGAACUG	7121
AD-2017422.1	caauagaaGfAfCfcacgaacugu	4160	PadCagdTudCguggdTcUfucuauuguu	5641	AACAAUAGAAGACCACGAACUGG	7122
AD-2017423.1	aauagaagAfCfCfacgaacuggu	4161	PadCcadGudTcgugdGuCfuucuauugu	5642	ACAAUAGAAGACCACGAACUGGU	7123
AD-2017424.1	auagaagaCfCfAfcgaacugguu	4162	PadAccdAgdTucgudGgUfcuucuauug	5643	CAAUAGAAGACCACGAACUGGUG	7124
AD-2017425.1	uagaagacCfAfCfgaacuggugu	4163	PadCacdCadGuucgdTgGfucuucuauu	5644	AAUAGAAGACCACGAACUGGUGA	7125
AD-2017426.1	agaagaccAfCfGfaacuggugau	4164	PadTcadCcdAguucdGuGfgucuucuau	5645	AUAGAAGACCACGAACUGGUGAU	7126
AD-2017427.1	gaagaccaCfGfAfacuggugauu	4165	PadAucdAcdCaguudCgUfggucuucua	5646	UAGAAGACCACGAACUGGUGAUU	7127
AD-2017428.1	aagaccacGfAfAfcuggugauuu	4166	PadAaudCadCcagudTcGfuggucuucu	5647	AGAAGACCACGAACUGGUGAUUG	7128
AD-2017429.1	agaccacgAfAfCfuggugauugu	4167	PadCaadTcdAccagdTuCfguggucuuc	5648	GAAGACCACGAACUGGUGAUUGA	7129
AD-2017430.1	gaccacgaAfCfUfggugauugau	4168	PadTcadAudCaccadGuUfcguggucuu	5649	AAGACCACGAACUGGUGAUUGAA	7130
AD-2017431.1	accacgaaCfUfGfgugauugaau	4169	PadTucdAadTcaccdAgUfucguggucu	5650	AGACCACGAACUGGUGAUUGAAG	7131
AD-2017432.1	ccacgaacUfGfGfugauugaagu	4170	PadCuudCadAucacdCaGfuucgugguc	5651	GACCACGAACUGGUGAUUGAAGU	7132
AD-2017433.1	cacgaacuGfGfUfgauugaaguu	4171	PadAcudTcdAaucadCcAfguucguggu	5652	ACCACGAACUGGUGAUUGAAGUG	7133
AD-2017434.1	gauagaagAfAfGfaaaacaaacu	4172	PadGuudTgdTuuucdTuCfuucuauccc	5653	GGGAUAGAAGAAGAAAACAAACU	7134
AD-2017435.1	auagaagaAfGfAfaaacaaacuu	4173	PadAgudTudGuuuudCuUfcuucuaucc	5654	GGAUAGAAGAAGAAAACAAACUA	7135
AD-2017436.1	uagaagaaGfAfAfaacaaacuau	4174	PadTagdTudTguuudTcUfucuucuauc	5655	GAUAGAAGAAGAAAACAAACUAU	7136
AD-2017437.1	gaagaagaAfAfAfcaaacuauau	4175	PadTaudAgdTuugudTuUfcuucuucua	5656	UAGAAGAAGAAAACAAACUAUAC	7137
AD-2017438.1	aagaagaaAfAfCfaaacuauacu	4176	PadGuadTadGuuugdTuUfucuucuucu	5657	AGAAGAAGAAAACAAACUAUACU	7138
AD-2017439.1	agaagaaaAfCfAfaacuauacuu	4177	PadAgudAudAguuudGuUfuucuucuuc	5658	GAAGAAGAAAACAAACUAUACUU	7139
AD-2017440.1	uucugaguUfCfAfagcacauauu	4178	PadAuadTgdTgcuudGaAfcucagaaac	5659	GUUUCUGAGUUCAAGCACAUAUC	7140
AD-2017441.1	ucugaguuCfAfAfgcacauaucu	4179	PadGaudAudGugcudTgAfacucagaaa	5660	UUUCUGAGUUCAAGCACAUAUCC	7141
AD-2017442.1	cugaguucAfAfGfcacauauccu	4180	PadGgadTadTgugcdTuGfaacucagaa	5661	UUCUGAGUUCAAGCACAUAUCCU	7142

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017443.1	ugaguucaAfGfCfacauauccuu	4181	PadAggdAudAugugdCuUfgaacucaga	5662	UCUGAGUUCAAGCACAUAUCCUG	7143
AD-2017444.1	gaguucaaGfCfAfcauauccugu	4182	PadCagdGadTaugudGcUfugaacucag	5663	CUGAGUUCAAGCACAUAUCCUGA	7144
AD-2017445.1	aguucaagCfAfCfauauccugau	4183	PadTcadGgdAuaugdTgCfuugaacuca	5664	UGAGUUCAAGCACAUAUCCUGAA	7145
AD-2017446.1	guucaagcAfCfAfuauccugaau	4184	PadTucdAgdGauaudGuGfcuugaacuc	5665	GAGUUCAAGCACAUAUCCUGAAA	7146
AD-2017447.1	uucaagcaCfAfUfauccugaaau	4185	PadTuudCadGgauadTgUfgcuugaacu	5666	AGUUCAAGCACAUAUCCUGAAAU	7147
AD-2017448.1	ucaagcacAfUfAfucugaaauu	4186	PadAuudTcdAggaudAuGfugcuugaac	5667	GUUCAAGCACAUAUCCUGAAAUU	7148
AD-2017449.1	caagcacaUfAfUfccugaaauuu	4187	PadAaudTudCaggadTaUfgugcuugaa	5668	UUCAAGCACAUAUCCUGAAAUUC	7149
AD-2017450.1	aagcacauAfUfCfcugaaauucu	4188	PadGaadTudTcaggdAuAfugugcuuga	5669	UCAAGCACAUAUCCUGAAAUUCA	7150
AD-2017451.1	agcacauaUfCfCfugaaauucau	4189	PadTgadAudTucagdGaUfaugugcuug	5670	CAAGCACAUAUCCUGAAAUUCAU	7151
AD-2017452.1	gcacauauCfCfUfgaaauucauu	4190	PadAugdAadTuucadGgAfuaugugcuu	5671	AAGCACAUAUCCUGAAAUUCAUG	7152
AD-2017453.1	cacauaucCfUfGfaauucaugu	4191	PadCaudGadAuuucdAgGfauaugugcu	5672	AGCACAUAUCCUGAAAUUCAUGG	7153
AD-2017454.1	acauauccUfGfAfaauucauggu	4192	PadCcadTgdAauuudCaGfgauaugugc	5673	GCACAUAUCCUGAAAUUCAUGGU	7154
AD-2017455.1	cauauccuGfAfAfauucaugguu	4193	PadAccdAudGaauudTcAfggauaugug	5674	CACAUAUCCUGAAAUUCAUGGUU	7155
AD-2017456.1	auauccugAfAfAfuucaugguuu	4194	PadAacdCadTgaaudTuCfaggauaugu	5675	ACAUAUCCUGAAAUUCAUGGUUU	7156
AD-2017457.1	uauccugaAfAfUfucaugguuuu	4195	PadAaadCcdAugaadTuUfcaggauaug	5676	CAUAUCCUGAAAUUCAUGGUUUC	7157
AD-2017458.1	uuuuucuaCfUfAfaaggaacauu	4196	PadAugdTudCcuuudAgUfagaaaaaua	5677	UAUUUUUCUACUAAAGGAACAUC	7158
AD-2017459.1	uuuucuacUfAfAfaggaacaucu	4197	PadGaudGudTccuudTaGfuagaaaaau	5678	AUUUUUCUACUAAAGGAACAUCA	7159
AD-2017460.1	uuucuacuAfAfAfggaacaucau	4198	PadTgadTgdTuccudTuAfguagaaaaa	5679	UUUUUCUACUAAAGGAACAUCAA	7160
AD-2017461.1	uucuacuaAfAfGfgaacaucaau	4199	PadTugdAudGuuccdTuUfaguagaaaa	5680	UUUUCUACUAAAGGAACAUCAAA	7161
AD-2017462.1	ucuacuaaAfGfGfaacaucaaau	4200	PadTuudGadTguucdCuUfuaguagaaa	5681	UUUCUACUAAAGGAACAUCAAAG	7162
AD-2017463.1	cuacuaaaGfGfAfacaucaaagu	4201	PadCuudTgdAuguudCcUfuuaguagaa	5682	UUCUACUAAAGGAACAUCAAAGG	7163
AD-2017464.1	uacuaaagGfAfAfcaucaaaggu	4202	PadCcudTudGaugudTcCfuuuaguaga	5683	UCUACUAAAGGAACAUCAAAGGA	7164
AD-2017465.1	acuaaaggAfAfCfaucaaaggau	4203	PadTccdTudTgaugdTuCfcuuuaguag	5684	CUACUAAAGGAACAUCAAAGGAA	7165
AD-2017466.1	cuaaaggaAfCfAfucaaaggaau	4204	PadTucdCudTugaudGuUfccuuuagua	5685	UACUAAAGGAACAUCAAAGGAAC	7166

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017467.1	uaaaggaaCfAfUfcaaaggaacu	4205	PadGuudCcdTuugadTgUfuccuuuagu	5686	ACUAAAGGAACAUCAAAGGAACC	7167
AD-2017468.1	aaaggaacAfUfCfaaaggaaccu	4206	PadGgudTcdCuuugdAuGfuuccuuuag	5687	CUAAAGGAACAUCAAAGGAACCG	7168
AD-2017469.1	aaggaacaUfCfAfaaggaaccgu	4207	PadCggdTudCcuuudGaUfguuccuuua	5688	UAAAGGAACAUCAAAGGAACCGC	7169
AD-2017470.1	aggaacauCfAfAfaggaaccgcu	4208	PadGcgdGudTccuudTgAfuguuccuuu	5689	AAAGGAACAUCAAAGGAACCGCG	7170
AD-2017471.1	ggaacaucAfAfAfggaaccgcgu	4209	PadCgcdGgdTuccudTuGfauguuccuu	5690	AAGGAACAUCAAAGGAACCGCGG	7171
AD-2017472.1	cacuggcaGfGfCfaaaaaaaau	4210	PadTuudTudTuuugdCcUfgccagugac	5691	GUCACUGGCAGGCAAAAAAAAAC	7172
AD-2017473.1	acuggcagGfCfAfaaaaaaacu	4211	PadGuudTudTuuuudGcCfugccaguga	5692	UCACUGGCAGGCAAAAAAAACA	7173
AD-2017474.1	cuggcaggCfAfAfaaaaaaacau	4212	PadTgudTudTuuuudTgCfcugccagug	5693	CACUGGCAGGCAAAAAAAACAU	7174
AD-2017475.1	uggcaggcAfAfAfaaaaaacauu	4213	PadAugdTudTuuuudTuGfccugccagu	5694	ACUGGCAGGCAAAAAAAACAUG	7175
AD-2017476.1	ggcaggcaAfAfAfaaaaacaugu	4214	PadCaudGudTuuuudTuUfgccugccag	5695	CUGGCAGGCAAAAAAAAACAUGG	7176
AD-2017477.1	gcaggcaaAfAfAfaaaacauggu	4215	PadCcadTgdTuuuudTuUfugccugcca	5696	UGGCAGGCAAAAAAAAACAUGGA	7177
AD-2017478.1	caggcaaaAfAfAfaaacauggau	4216	PadTccdAudGuuuudTuUfuugccugcc	5697	GGCAGGCAAAAAAAAACAUGGAG	7178
AD-2017479.1	aggcaaaaAfAfAfaacauggagu	4217	PadCucdCadTguuudTuUfuuugccugc	5698	GCAGGCAAAAAAAAACAUGGAGC	7179
AD-2017480.1	ggcaaaaaAfAfAfacauggagcu	4218	PadGcudCcdAuguudTuUfuuuugccug	5699	CAGGCAAAAAAAAACAUGGAGCA	7180
AD-2017481.1	gcaaaaaaAfAfAfcauggagcau	4219	PadTgcdTcdCaugudTuUfuuuuugccu	5700	AGGCAAAAAAAAACAUGGAGCAC	7181
AD-2017482.1	caaaaaaaAfAfCfauggagcacu	4220	PadGugdCudCcaugdTuUfuuuuuugcc	5701	GGCAAAAAAAAACAUGGAGCACC	7182
AD-2017483.1	aaaaaaaaAfCfAfuggagcaccu	4221	PadGgudGcdTccaudGuUfuuuuuuugc	5702	GCAAAAAAAAACAUGGAGCACCG	7183
AD-2017484.1	aaaaaaaaCfAfUfggagcaccgu	4222	PadCggdTgdCuccadTgUfuuuuuuuug	5703	CAAAAAAAAACAUGGAGCACCGA	7184
AD-2017485.1	aaaaaaacAfUfGfgagcaccgau	4223	PadTcgdGudGcuccdAuGfuuuuuuuuu	5704	AAAAAAAAACAUGGAGCACCGAC	7185
AD-2017486.1	aaaaaacaUfGfGfagcaccgacu	4224	PadGucdGgdTgcucdCaUfguuuuuuuu	5705	AAAAAAAACAUGGAGCACCGACU	7186
AD-2017487.1	aaaaacauGfGfAfgcaccgacuu	4225	PadAgudCgdGugcudCcAfuguuuuuuu	5706	AAAAAAACAUGGAGCACCGACUA	7187
AD-2017488.1	aaaacaugGfAfGfcaccgacuau	4226	PadTagdTcdGgugcdTcCfauguuuuuu	5707	AAAAAACAUGGAGCACCGACUAA	7188
AD-2017489.1	aaacauggAfGfCfaccgacuaau	4227	PadTuadGudCggugdCuCfcauguuuuu	5708	AAAAACAUGGAGCACCGACUAAC	7189
AD-2017490.1	cugaagccCfUfUfucaguugcgu	4228	PadCgcdAadCugaadAgGfgcuucagug	5709	CACUGAAGCCCUUUCAGUUGCGG	7190

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017491.1	ugaagcccUfUfUfcaguugcggu	4229	PadCcgdCadAcugadAaGfggcuucagu	5710	ACUGAAGCCCUUUCAGUUGCGGU	7191
AD-2017492.1	gaagcccuUfUfCfaguugcgguu	4230	PadAccdGcdAacugdAaAfgggcuucag	5711	CUGAAGCCCUUUCAGUUGCGGUU	7192
AD-2017493.1	aagcccuuUfCfAfguugcgguuu	4231	PadAacdCgdCaacudGaAfagggcuuca	5712	UGAAGCCCUUUCAGUUGCGGUUG	7193
AD-2017494.1	agcccuuuCfAfGfuugcgguugu	4232	PadCaadCcdGcaacdTgAfaagggcuuc	5713	GAAGCCCUUUCAGUUGCGGUUGA	7194
AD-2017495.1	gcccuuucAfGfUfugcgguugau	4233	PadTcadAcdCgcaadCuGfaaagggcuu	5714	AAGCCCUUUCAGUUGCGGUUGAA	7195
AD-2017496.1	cccuuucaGfUfUfgcgguugaau	4234	PadTucdAadCcgcadAcUfgaaagggcu	5715	AGCCCUUUCAGUUGCGGUUGAAG	7196
AD-2017497.1	ccuuucagUfUfGfcgguugaagu	4235	PadCuudCadAccgcdAaCfugaaagggc	5716	GCCCUUUCAGUUGCGGUUGAAGA	7197
AD-2017498.1	cuuucaguUfGfCfgguugaagau	4236	PadTcudTcdAaccgdCaAfcugaaaggg	5717	CCCUUUCAGUUGCGGUUGAAGAA	7198
AD-2017499.1	uuucaguuGfCfGfguugaagaau	4237	PadTucdTudCaaccdGcAfacugaaagg	5718	CCUUUCAGUUGCGGUUGAAGAAG	7199
AD-2017500.1	uucaguugCfGfGfugaagaagu	4238	PadCuudCudTcaacdCgCfaacugaaag	5719	CUUUCAGUUGCGGUUGAAGAAGG	7200
AD-2017501.1	ucaguugcGfGfUfugaagaaggu	4239	PadCcudTcdTucaadCcGfcaacugaaa	5720	UUUCAGUUGCGGUUGAAGAAGGA	7201
AD-2017502.1	caguugcgGfUfUfgaagaaggau	4240	PadTccdTudCuucadAcCfgcaacugaa	5721	UUCAGUUGCGGUUGAAGAAGGAC	7202
AD-2017503.1	aguugcggUfUfGfaagaaggacu	4241	PadGucdCudTcuucdAaCfcgcaacuga	5722	UCAGUUGCGGUUGAAGAAGGACU	7203
AD-2017504.1	guugcgguUfGfAfagaaggacuu	4242	PadAgudCcdTucuudCaAfccgcaacug	5723	CAGUUGCGGUUGAAGAAGGACUC	7204
AD-2017505.1	uugcgguuGfAfAfgaaggacucu	4243	PadGagdTcdCuucudTcAfaccgcaacu	5724	AGUUGCGGUUGAAGAAGGACUCG	7205
AD-2017506.1	ugcgguugAfAfGfaaggacucgu	4244	PadCgadGudCcuucdTuCfaaccgcaac	5725	GUUGCGGUUGAAGAAGGACUCGC	7206
AD-2017507.1	gcgguugaAfGfAfaggacucgcu	4245	PadGcgdAgdTccuudCuUfcaaccgcaa	5726	UUGCGGUUGAAGAAGGACUCGCU	7207
AD-2017508.1	cgguugaaGfAfAfggacucgcuu	4246	PadAgcdGadGuccudTcUfucaaccgca	5727	UGCGGUUGAAGAAGGACUCGCUU	7208
AD-2017509.1	gguugaagAfAfGfgacucgcuuu	4247	PadAagdCgdAguccdTuCfuucaaccgc	5728	GCGGUUGAAGAAGGACUCGCUUG	7209
AD-2017510.1	guugaagaAfGfGfacucgcuugu	4248	PadCaadGcdGagucdCuUfcuucaaccg	5729	CGGUUGAAGAAGGACUCGCUUGG	7210
AD-2017511.1	uugaagaaGfGfAfcucgcuuggu	4249	PadCcadAgdCgagudCcUfucuucaacc	5730	GGUUGAAGAAGGACUCGCUUGGA	7211
AD-2017512.1	ugaagaagGfAfCfucgcuuggau	4250	PadTccdAadGcgagdTcCfuucuucaac	5731	GUUGAAGAAGGACUCGCUUGGAG	7212
AD-2017513.1	gaagaaggAfCfUfcgcuuggagu	4251	PadCucdCadAgcgadGuCfcuucuucaa	5732	UUGAAGAAGGACUCGCUUGGAGG	7213
AD-2017514.1	aagaaggaCfUfCfgcuuggaggu	4252	PadCcudCcdAagcgdAgUfccuucuuca	5733	UGAAGAAGGACUCGCUUGGAGGA	7214

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017515.1	agaaggacUfCfGfcuuggaggau	4253	PadTccdTcdCaagcdGaGfuccuucuuc	5734	GAAGAAGGACUCGCUUGGAGGAA	7215
AD-2017516.1	gaaggacuCfGfCfuuggaggaau	4254	PadTucdCudCcaagdCgAfguccuucuu	5735	AAGAAGGACUCGCUUGGAGGAAA	7216
AD-2017517.1	cugccucuUfCfAfcagagcucuu	4255	PadAgadGcdTcugudGaAfgaggcagug	5736	CACUGCCUCUUCACAGAGCUCUG	7217
AD-2017518.1	ugccucuuCfAfCfagagcucugu	4256	PadCagdAgdCucugdTgAfagaggcagu	5737	ACUGCCUCUUCACAGAGCUCUGC	7218
AD-2017519.1	gccucuucAfCfAfgagcucugcu	4257	PadGcadGadGcucudGuGfaagaggcag	5738	CUGCCUCUUCACAGAGCUCUGCC	7219
AD-2017520.1	ccucuucaCfAfGfagcucugccu	4258	PadGgcdAgdAgcucdTgUfgaagaggca	5739	UGCCUCUUCACAGAGCUCUGCCA	7220
AD-2017521.1	cucuucacAfGfAfgcucugccau	4259	PadTggdCadGagcudCuGfugaagaggc	5740	GCCUCUUCACAGAGCUCUGCCAC	7221
AD-2017522.1	ucuucacaGfAfGfcucugccacu	4260	PadGugdGcdAgagcdTcUfgugaagagg	5741	CCUCUUCACAGAGCUCUGCCACA	7222
AD-2017523.1	cuucacagAfGfCfucugccacau	4261	PadTgudGgdCagagdCuCfugugaagag	5742	CUCUUCACAGAGCUCUGCCACAA	7223
AD-2017524.1	uucacagaGfCfUfcugccacaau	4262	PadTugdTgdGcagadGcUfcugugaaga	5743	UCUUCACAGAGCUCUGCCACAAA	7224
AD-2017525.1	ucacagagCfUfCfugccacaaau	4263	PadTuudGudGgcagdAgCfucugugaag	5744	CUUCACAGAGCUCUGCCACAAAC	7225
AD-2017526.1	cacagagcUfCfUfgccacaaacu	4264	PadGuudTgdTggcadGaGfcucugugaa	5745	UUCACAGAGCUCUGCCACAAACA	7226
AD-2017527.1	acagagcuCfUfGfccacaaacau	4265	PadTgudTudGuggcdAgAfgcucuguga	5746	UCACAGAGCUCUGCCACAAACAU	7227
AD-2017528.1	cagagcucUfGfCfcacaaacauu	4266	PadAugdTudTguggdCaGfagcucugug	5747	CACAGAGCUCUGCCACAAACAUG	7228
AD-2017529.1	agagcucuGfCfCfacaaacaugu	4267	PadCaudGudTugugdGcAfgagcucugu	5748	ACAGAGCUCUGCCACAAACAUGG	7229
AD-2017530.1	gagcucugCfCfAfcaaacauggu	4268	PadCcadTgdTuugudGgCfagagcucug	5749	CAGAGCUCUGCCACAAACAUGGC	7230
AD-2017531.1	agcucugcCfAfCfaaacauggcu	4269	PadGccdAudGuuugdTgGfcagagcucu	5750	AGAGCUCUGCCACAAACAUGGCU	7231
AD-2017532.1	gcucugccAfCfAfaacauggcuu	4270	PadAgcdCadTguuudGuGfgcagagcuc	5751	GAGCUCUGCCACAAACAUGGCUA	7232
AD-2017533.1	cucugccaCfAfAfacauggcuau	4271	PadTagdCcdAuguudTgUfggcagagcu	5752	AGCUCUGCCACAAACAUGGCUAU	7233
AD-2017534.1	ucugccacAfAfAfcauggcuauu	4272	PadAuadGcdCaugudTuGfuggcagagc	5753	GCUCUGCCACAAACAUGGCUAUC	7234
AD-2017535.1	gauuuacaGfAfUfcuaauacagu	4273	PadCugdTadTuagadTcUfguaaaucuu	5754	AAGAUUUACAGAUCUAAUACAGC	7235
AD-2017536.1	auuuacagAfUfCfuaauacagcu	4274	PadGcudGudAuuagdAuCfuguaaaucu	5755	AGAUUUACAGAUCUAAUACAGCU	7236
AD-2017537.1	uuuacagaUfCfUfaauacagcuu	4275	PadAgcdTgdTauuadGaUfcuguaaauc	5756	GAUUUACAGAUCUAAUACAGCUG	7237
AD-2017538.1	uuacagauCfUfAfauacagcugu	4276	PadCagdCudGuauudAgAfucuguaaau	5757	AUUUACAGAUCUAAUACAGCUGG	7238

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017539.1	uacagaucUfAfAfu acagcuggu	4277	PadCcadGcdTguaudTa Gfaucuguaaa	5758	UUUACAGAUCUAA UACAGCUGGU	7239
AD-2017540.1	acagaucuAfAfUfac agcugguu	4278	PadAccdAgdCuguadT uAfgaucuguaa	5759	UUACAGAUCUAAU ACAGCUGGUG	7240
AD-2017541.1	cagaucuaAfUfAfca gcuggugu	4279	PadCacdCadGcugudA uUfagaucugua	5760	UACAGAUCUAAUA CAGCUGGUGG	7241
AD-2017542.1	agaucuaaUfAfCfag cugguggu	4280	PadCcadCcdAgcugdTa Ufuagaucugu	5761	ACAGAUCUAAUAC AGCUGGUGGA	7242
AD-2017543.1	gaucuaauAfCfAfg cugguggau	4281	PadTccdAcdCagcudGu Afuuagaucug	5762	CAGAUCUAAUACA GCUGGUGGAG	7243
AD-2017544.1	aucuaauaCfAfGfcu gguggagu	4282	PadCucdCadCcagcdTg Ufauuagaucu	5763	AGAUCUAAUACAG CUGGUGGAGU	7244
AD-2017545.1	ucuaauacAfGfCfu gguggaguu	4283	PadAcudCcdAccagdC uGfuauuagauc	5764	GAUCUAAUACAGC UGGUGGAGUU	7245
AD-2017546.1	cuaauacaGfCfUfgg uggaguuu	4284	PadAacdTcdCaccadGc Ufguauuagau	5765	AUCUAAUACAGCU GGUGGAGUUC	7246
AD-2017547.1	uaauacagCfUfGfg uggaguucu	4285	PadGaadCudCcaccdAg Cfuguauuaga	5766	UCUAAUACAGCUG GUGGAGUUCU	7247
AD-2017548.1	aauacagcUfGfGfu ggaguucuu	4286	PadAgadAcdTccacdCa Gfcuguauuag	5767	CUAAUACAGCUGG UGGAGUUCUA	7248
AD-2017549.1	auacagcuGfGfUfg gaguucuau	4287	PadTagdAadCuccadCc Afgcuguauua	5768	UAAUACAGCUGGU GGAGUUCUAU	7249
AD-2017550.1	uacagcugGfUfGfg aguucuauu	4288	PadAuadGadAcuccdA cCfagcuguauu	5769	AAUACAGCUGGUG GAGUUCUAUC	7250
AD-2017551.1	acagcuggUfGfGfa guucuaucu	4289	PadGaudAgdAacucdC aCfcagcuguau	5770	AUACAGCUGGUGG AGUUCUAUCA	7251
AD-2017552.1	cagcugguGfGfAfg uucuaucau	4290	PadTgadTadGaacudCc Afccagcugua	5771	UACAGCUGGUGGA GUUCUAUCAA	7252
AD-2017553.1	ugcuaggaUfUfGfc ucucuagau	4291	PadTcudAgdAgagcdA aUfccuagcaca	5772	UGUGCUAGGAUUG CUCUCUAGAC	7253
AD-2017554.1	gcuaggauUfGfCfu cucuagacu	4292	PadGucdTadGagagdCa Afuccuagcac	5773	GUGCUAGGAUUGC UCUCUAGACA	7254
AD-2017555.1	cuaggauuGfCfUfc ucuagacau	4293	PadTgudCudAgagadG cAfauccuagca	5774	UGCUAGGAUUGCU CUCUAGACAA	7255
AD-2017556.1	uaggauugCfUfCfu cuagacaau	4294	PadTugdTcdTagagdAg Cfaauccuagc	5775	GCUAGGAUUGCUC UCUAGACAAG	7256
AD-2017557.1	aggauugcUfCfUfc uagacaagu	4295	PadCuudGudCuagadG aGfcaauccuag	5776	CUAGGAUUGCUCU CUAGACAAGC	7257
AD-2017558.1	ggauugcuCfUfCfu agacaagcu	4296	PadGcudTgdTcuagdA gAfgcaauccua	5777	UAGGAUUGCUCUC UAGACAAGCC	7258
AD-2017559.1	gauugcucUfCfUfa gacaagccu	4297	PadGgcdTudGucuadG aGfagcaauccu	5778	AGGAUUGCUCUCU AGACAAGCCA	7259
AD-2017560.1	auugcucuCfUfAfg acaagccau	4298	PadTggdCudTgucudA gAfgagcaaucc	5779	GGAUUGCUCUCUA GACAAGCCAG	7260
AD-2017561.1	uugcucucUfAfGfa caagccagu	4299	PadCugdGcdTugucdTa Gfagagcaauc	5780	GAUUGCUCUCUAG ACAAGCCAGA	7261
AD-2017562.1	ugcucucuAfGfAfc aagccagau	4300	PadTcudGgdCuugudC uAfgagagcaau	5781	AUUGCUCUCUAGA CAAGCCAGAA	7262

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017563.1	gcucucuaGfAfCfaagccagaau	4301	PadTucdTgdGcuugdTcUfagagagcaa	5782	UUGCUCUCUAGACAAGCCAGAAG	7263
AD-2017564.1	cucucuagAfCfAfagccagaagu	4302	PadCuudCudGgcuudGuCfuagagagca	5783	UGCUCUCUAGACAAGCCAGAAGU	7264
AD-2017565.1	ucucuagaCfAfAfgccagaaguu	4303	PadAcudTcdTggcudTgUfcuagagagc	5784	GCUCUCUAGACAAGCCAGAAGUG	7265
AD-2017566.1	cucuagacAfAfGfccagaagugu	4304	PadCacdTudCuggcdTuGfucuagagag	5785	CUCUCUAGACAAGCCAGAAGUGA	7266
AD-2017567.1	ucuagacaAfGfCfcagaagugau	4305	PadTcadCudTcuggdCuUfgucuagaga	5786	UCUCUAGACAAGCCAGAAGUGAC	7267
AD-2017568.1	cuagacaaGfCfCfagaagugacu	4306	PadGucdAcdTucugdGcUfugucuagag	5787	CUCUAGACAAGCCAGAAGUGACU	7268
AD-2017569.1	uagacaagCfCfAfgaagugacuu	4307	PadAgudCadCuucudGgCfuugucuaga	5788	UCUAGACAAGCCAGAAGUGACUU	7269
AD-2017570.1	agacaagcCfAfGfaagugacuuu	4308	PadAagdTcdAcuucdTgGfcuugucuag	5789	CUAGACAAGCCAGAAGUGACUUA	7270
AD-2017571.1	gacaagccAfGfAfagugacuuau	4309	PadTaadGudCacuudCuGfgcuugucua	5790	UAGACAAGCCAGAAGUGACUUAU	7271
AD-2017572.1	acaagccaGfAfAfgugacuuauu	4310	PadAuadAgdTcacudTcUfggcuugucu	5791	AGACAAGCCAGAAGUGACUUAUU	7272
AD-2017573.1	caagccagAfAfGfugacuuauuu	4311	PadAaudAadGucacdTuCfuggcuuguc	5792	GACAAGCCAGAAGUGACUUAUUA	7273
AD-2017574.1	aagccagaAfGfUfgacuuauuau	4312	PadTaadTadAgucadCuUfcuggcuugu	5793	ACAAGCCAGAAGUGACUUAUUAA	7274
AD-2017575.1	acuuauuaAfAfCfuauugaaggu	4313	PadCcudTcdAauagdTuUfaauaaguca	5794	UGACUUAUUAAACUAUUGAAGGA	7275
AD-2017576.1	cuuauuaaAfCfUfauugaaggau	4314	PadTccdTudCaauadGuUfuaauaaguc	5795	GACUUAUUAAACUAUUGAAGGAA	7276
AD-2017577.1	uuaaacuaUfUfGfaaggaaaagu	4315	PadCuudTudCcuucdAaUfaguuuaaua	5796	UAUUAAACUAUUGAAGGAAAAGG	7277
AD-2017578.1	uaaacuauUfGfAfaggaaaaggu	4316	PadCcudTudTccuudCaAfuaguuuaau	5797	AUUAAACUAUUGAAGGAAAAGGA	7278
AD-2017579.1	aaacuauuGfAfAfggaaaaggau	4317	PadTccdTudTuccudTcAfauaguuuaa	5798	UUAAACUAUUGAAGGAAAAGGAC	7279
AD-2017580.1	aacuauugAfAfGfgaaaaggacu	4318	PadGucdCudTuuccdTuCfaauaguuua	5799	UAAACUAUUGAAGGAAAAGGACU	7280
AD-2017581.1	acuauugaAfGfGfaaaaggacuu	4319	PadAgudCcdTuuucdCuUfcaauaguuu	5800	AAACUAUUGAAGGAAAAGGACUC	7281
AD-2017582.1	cuauugaaGfGfAfaaaggacucu	4320	PadGagdTcdCuuuudCcUfucaauaguu	5801	AACUAUUGAAGGAAAAGGACUCA	7282
AD-2017583.1	uauugaagGfAfAfaaggacucau	4321	PadTgadGudCcuuudTcCfuucaauagu	5802	ACUAUUGAAGGAAAAGGACUCAA	7283
AD-2017584.1	auugaaggAfAfAfaggacucaau	4322	PadTugdAgdTccuudTuCfcuucaauag	5803	CUAUUGAAGGAAAAGGACUCAAG	7284
AD-2017585.1	uugaaggaAfAfAfggacucaagu	4323	PadCuudGadGuccudTuUfccuucaaua	5804	UAUUGAAGGAAAAGGACUCAAGA	7285
AD-2017586.1	ugaaggaaAfAfGfgacucaagau	4324	PadTcudTgdAguccdTuUfuccuucaau	5805	AUUGAAGGAAAAGGACUCAAGAA	7286

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017587.1	gaaggaaaAfGfGfacucaagaau	4325	PadTucdTudGagucdCuUfuuccuucaa	5806	UUGAAGGAAAAGGACUCAAGAAA	7287
AD-2017588.1	aaggaaaaGfGfAfcucaagaaau	4326	PadTuudCudTgagudCcUfuuuccuuca	5807	UGAAGGAAAAGGACUCAAGAAAA	7288
AD-2017589.1	aggaaaagGfAfCfucaagaaaau	4327	PadTuudTcdTugagdTcCfuuuuccuuc	5808	GAAGGAAAAGGACUCAAGAAAAA	7289
AD-2017590.1	aaaagaccAfUfAfaauaagggcu	4328	PadGccdCudTauuudAuGfgucuuuuau	5809	AUAAAAGACCAUAAAUAAGGGCG	7290
AD-2017591.1	augugaaaAfGfAfauguauuucu	4329	PadGaadAudAcauudCuUfuucacaugg	5810	CCAUGUGAAAAGAAUGUAUUUCA	7291
AD-2017592.1	ugugaaaaGfAfAfuguauuucau	4330	PadTgadAadTacaudTcUfuuucacaug	5811	CAUGUGAAAAGAAUGUAUUUCAC	7292
AD-2017593.1	gugaaaagAfAfUfguauuucacu	4331	PadGugdAadAuacadTuCfuuuucacau	5812	AUGUGAAAAGAAUGUAUUUCACC	7293
AD-2017594.1	ugaaaagaAfUfGfuauuucaccu	4332	PadGgudGadAauacdAuUfcuuuucaca	5813	UGUGAAAAGAAUGUAUUUCACCU	7294
AD-2017595.1	gaaaagaaUfGfUfauuucaccuu	4333	PadAggdTgdAaauadCaUfucuuuucac	5814	GUGAAAAGAAUGUAUUUCACCUG	7295
AD-2017596.1	aaaagaauGfUfAfuuucaccugu	4334	PadCagdGudGaaaudAcAfuucuuuuca	5815	UGAAAAGAAUGUAUUUCACCUGC	7296
AD-2017597.1	aaagaaugUfAfUfucaccugcu	4335	PadGcadGgdTgaaadTaCfauucuuuuc	5816	GAAAAGAAUGUAUUUCACCUGCA	7297
AD-2017598.1	aagaauguAfUfUfucaccugcau	4336	PadTgcdAgdGugaadAuAfcauucuuuu	5817	AAAAGAAUGUAUUUCACCUGCAA	7298
AD-2017599.1	agaauguaUfUfUfcaccugcaau	4337	PadTugdCadGgugadAaUfacauucuuu	5818	AAAGAAUGUAUUUCACCUGCAAG	7299
AD-2017600.1	gaauguauUfUfCfaccugcaagu	4338	PadCuudGcdAggugdAaAfuacauucuu	5819	AAGAAUGUAUUUCACCUGCAAGU	7300
AD-2017601.1	aauguauuUfCfAfccugcaaguu	4339	PadAcudTgdCaggudGaAfauacauucu	5820	AGAAUGUAUUUCACCUGCAAGUU	7301
AD-2017602.1	auguauuuCfAfCfcugcaaguuu	4340	PadAacdTudGcaggdTgAfaauacauuc	5821	GAAUGUAUUUCACCUGCAAGUUA	7302
AD-2017603.1	uguauuucAfCfCfugcaaguuau	4341	PadTaadCudTgcagdGuGfaaauacauu	5822	AAUGUAUUUCACCUGCAAGUUAC	7303
AD-2017604.1	guauuucaCfCfUfgcaaguuacu	4342	PadGuadAcdTugcadGgUfgaaauacau	5823	AUGUAUUUCACCUGCAAGUUACA	7304
AD-2017605.1	uauuucacCfUfGfcaaguuacau	4343	PadTgudAadCuugcdAgGfugaaauaca	5824	UGUAUUUCACCUGCAAGUUACAA	7305
AD-2017606.1	auuucaccUfGfCfaaguuacaau	4344	PadTugdTadAcuugdCaGfgugaaauac	5825	GUAUUUCACCUGCAAGUUACAAA	7306
AD-2017607.1	uuucaccuGfCfAfaguuacaaau	4345	PadTuudGudAacuudGcAfggugaaaua	5826	UAUUUCACCUGCAAGUUACAAAA	7307
AD-2017608.1	uucaccugCfAfAfguuacaaaau	4346	PadTuudTgdTaacudTgCfaggugaaau	5827	AUUUCACCUGCAAGUUACAAAAA	7308
AD-2017609.1	ccugcaagUfUfAfcaaaaaauu	4347	PadAuudTudTuugudAaCfuugcaggug	5828	CACCUGCAAGUUACAAAAAAUA	7309
AD-2017610.1	cugcaaguUfAfCfaaaaaauau	4348	PadTaudTudTuuugdTaAfcuugcaggu	5829	ACCUGCAAGUUACAAAAAAUAG	7310

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017611.1	ugcaaguuAfCfAfaaaaaauagu	4349	PadCuadTudTuuuudGuAfacuugcagg	5830	CCUGCAAGUUACAAAAAAAUAGU	7311
AD-2017612.1	gcaaguuaCfAfAfaaaaauaguu	4350	PadAcudAudTuuuudTgUfaacuugcag	5831	CUGCAAGUUACAAAAAAAUAGUU	7312
AD-2017613.1	aaguuacaAfAfAfaaauaguuuu	4351	PadAaadCudAuuuudTuUfguaacuugc	5832	GCAAGUUACAAAAAAAUAGUUUG	7313
AD-2017614.1	uuacaaaaAfAfAfuaguuugugu	4352	PadCacdAadAcuaudTuUfuuuguaacu	5833	AGUUACAAAAAAAUAGUUUGUGC	7314
AD-2017615.1	uacaaaaaAfAfUfaguuugugcu	4353	PadGcadCadAacuadTuUfuuuuguaac	5834	GUUACAAAAAAAUAGUUUGUGCA	7315
AD-2017616.1	aaaccuuaGfGfAfaaaaaaugau	4354	PadTcadTudTuuuudCcUfaagguuuaa	5835	UUAAACCUUAGGAAAAAAAUGAC	7316
AD-2017617.1	aaccuuagGfAfAfaaaaaugacu	4355	PadGucdAudTuuuudTcCfuaagguuua	5836	UAAACCUUAGGAAAAAAAUGACU	7317
AD-2017618.1	accuuaggAfAfAfaaaaaugacuu	4356	PadAgudCadTuuuudTuCfcuaagguuu	5837	AAACCUUAGGAAAAAAAUGACUU	7318
AD-2017619.1	ccuuaggaAfAfAfaaaaugacuuu	4357	PadAagdTcdAuuuudTuUfccuaagguu	5838	AACCUUAGGAAAAAAAUGACUUG	7319
AD-2017620.1	cuuaggaaAfAfAfaaaugacuugu	4358	PadCaadGudCauuudTuUfuccuaaggu	5839	ACCUUAGGAAAAAAAUGACUUGG	7320
AD-2017621.1	uuaggaaaAfAfAfaugacuuggu	4359	PadCcadAgdTcauudTuUfuuccuaagg	5840	CCUUAGGAAAAAAAUGACUUGGU	7321
AD-2017622.1	uaggaaaaAfAfAfugacuugguu	4360	PadAccdAadGucaudTuUfuuuccuaag	5841	CUUAGGAAAAAAAUGACUUGGUG	7322
AD-2017623.1	aggaaaaaAfAfUfgacuuggugu	4361	PadCacdCadAgucadTuUfuuuuccuaa	5842	UUAGGAAAAAAAUGACUUGGUGU	7323
AD-2017624.1	ggaaaaaaAfUfGfacuugguguu	4362	PadAcadCcdAagucdAuUfuuuuuccua	5843	UAGGAAAAAAAUGACUUGGUGUG	7324
AD-2017625.1	gaaaaaaaUfGfAfcuugguguu	4363	PadCacdAcdCaagudCaUfuuuuuuccu	5844	AGGAAAAAAAUGACUUGGUGUGU	7325
AD-2017626.1	aaaaaaauGfAfCfuuggugugu	4364	PadAcadCadCcaagdTcAfuuuuuuucc	5845	GGAAAAAAAUGACUUGGUGUGUU	7326
AD-2017627.1	aaaaaaugAfCfUfuggugugu	4365	PadAacdAcdAccaadGuCfauuuuuuuc	5846	GAAAAAAAUGACUUGGUGUGUUC	7327
AD-2017628.1	aaaaaugaCfUfUfggugugucu	4366	PadGaadCadCaccadAgUfcauuuuuuu	5847	AAAAAAAUGACUUGGUGUGUUCU	7328
AD-2017629.1	aaaaugacUfUfGfgugugucuu	4367	PadAgadAcdAcaccdAaGfucauuuuuu	5848	AAAAAAUGACUUGGUGUGUUCUU	7329
AD-2017630.1	aaaugacuUfGfGfuguguucuu	4368	PadAagdAadCacacdCaAfgucauuuuu	5849	AAAAAUGACUUGGUGUGUUCUUG	7330
AD-2017631.1	aaugacuuGfGfUfguguucuugu	4369	PadCaadGadAcacadCcAfagucauuuu	5850	AAAAUGACUUGGUGUGUUCUUGU	7331
AD-2017632.1	augacuugGfUfGfuguucuuguu	4370	PadAcadAgdAacacdAcCfaagucauuu	5851	AAAUGACUUGGUGUGUUCUUGUG	7332
AD-2017633.1	ugacuuggUfGfUfguucuugugu	4371	PadCacdAadGaacadCaCfcaagucauu	5852	AAUGACUUGGUGUGUUCUUGUGU	7333
AD-2017634.1	gacuugguGfUfGfucuuguguu	4372	PadAcadCadAgaacdAcAfccaagucau	5853	AUGACUUGGUGUGUUCUUGUGUG	7334

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017635.1	acuuggugUfGfUfucuugugugu	4373	PadCacdAcdAagaadCaCfaccaaguca	5854	UGACUUGGUGUGUUCUUGUGUGA	7335
AD-2017636.1	cuugguguGfUfUfcuugugugau	4374	PadTcadCadCaagadAcAfcaccaaguc	5855	GACUUGGUGUGUUCUUGUGUGAU	7336
AD-2017637.1	uuggugugUfUfCfuugugugauu	4375	PadAucdAcdAcaagdAaCfacaccaagu	5856	ACUUGGUGUGUUCUUGUGUGAUU	7337
AD-2017638.1	ugguguguUfCfUfugugugauuu	4376	PadAaudCadCacaadGaAfcacaccaag	5857	CUUGGUGUGUUCUUGUGUGAUUU	7338
AD-2017639.1	gguguguuCfUfUfgugugauuuu	4377	PadAaadTcdAcacadAgAfacacaccaa	5858	UUGGUGUGUUCUUGUGUGAUUUU	7339
AD-2017640.1	guguguucUfUfGfugugauuuuu	4378	PadAaadAudCacacdAaGfaacacacca	5859	UGGUGUGUUCUUGUGUGAUUUUU	7340
AD-2017641.1	uguguucuUfGfUfgugauuuuuu	4379	PadAaadAadTcacadCaAfgaacacacc	5860	GGUGUGUUCUUGUGUGAUUUUUA	7341
AD-2017642.1	guguucuuGfUfGfugauuuuuau	4380	PadTaadAadAucacdAcAfagaacacac	5861	GUGUGUUCUUGUGUGAUUUUUAC	7342
AD-2017643.1	uguucuugUfGfUfgauuuuuacu	4381	PadGuadAadAaucadCaCfaagaacaca	5862	UGUGUUCUUGUGUGAUUUUUACA	7343
AD-2017644.1	guucuuguGfUfGfauuuuuacau	4382	PadTgudAadAaaucdAcAfcaagaacac	5863	GUGUUCUUGUGUGAUUUUUACAU	7344
AD-2017645.1	uucuugugUfGfAfuuuuuacauu	4383	PadAugdTadAaaaudCaCfacaagaaca	5864	UGUUCUUGUGUGAUUUUUACAUU	7345
AD-2017646.1	ucuuguguGfAfUfuuuuacauuu	4384	PadAaudGudAaaaadTcAfcacaagaac	5865	GUUCUUGUGUGAUUUUUACAUUG	7346
AD-2017647.1	cuugugugAfUfUfuuuacauugu	4385	PadCaadTgdTaaaadAuCfacacaagaa	5866	UUCUUGUGUGAUUUUUACAUUGC	7347
AD-2017648.1	uugugugaUfUfUfuuacauugcu	4386	PadGcadAudGuaaadAaUfcacacaaga	5867	UCUUGUGUGAUUUUUACAUUGCU	7348
AD-2017649.1	ugugugauUfUfUfuacauugcuu	4387	PadAgcdAadTguaadAaAfucacacaag	5868	CUUGUGUGAUUUUUACAUUGCUA	7349
AD-2017650.1	gugugauuUfUfUfacauugcuau	4388	PadTagdCadAuguadAaAfaucacacaa	5869	UUGUGUGAUUUUUACAUUGCUAU	7350
AD-2017651.1	ugugauuuUfUfAfcauugcuauu	4389	PadAuadGcdAaugudAaAfaaucacaca	5870	UGUGUGAUUUUUACAUUGCUAUA	7351
AD-2017652.1	gugauuuuUfAfCfauugcuauau	4390	PadTaudAgdCaaugdTaAfaaaucacac	5871	GUGUGAUUUUUACAUUGCUAUAA	7352
AD-2017653.1	ugcauauuUfAfAfaacaugucuu	4391	PadAgadCadTguuudTaAfauaugcaua	5872	UAUGCAUAUUUUAAAACAUGUCUC	7353
AD-2017654.1	gcauauuuAfAfAfacaugucucu	4392	PadGagdAcdAuguudTuAfaauaugcau	5873	AUGCAUAUUUAAAACAUGUCUCC	7354
AD-2017655.1	cauauuuaAfAfAfcaugucuccu	4393	PadGgadGadCaugudTuUfaaauaugca	5874	UGCAUAUUUAAAACAUGUCUCCC	7355
AD-2017656.1	auauuuaaAfAfCfaugucucccu	4394	PadGggdAgdAcaugdTuUfuaaauaugc	5875	GCAUAUUUAAAACAUGUCUCCCU	7356
AD-2017657.1	uauuuaaaAfCfAfugucucccuu	4395	PadAggdGadGacaudGuUfuuaaaauag	5876	CAUAUUUAAAACAUGUCUCCCUU	7357
AD-2017658.1	auuuaaaaCfAfUfgucucccuuu	4396	PadAagdGgdAgacadTgUfuuuaaauau	5877	AUAUUUAAAACAUGUCUCCCUUA	7358

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017659.1	uuuaaaacAfUfGfucucccuuau	4397	PadTaadGgdGagacdAuGfuuuuaaaua	5878	UAUUUAAAACAUGUCUCCCUUAU	7359
AD-2017660.1	uuaaaacaUfGfUfcucccuuauu	4398	PadAuadAgdGgagadCaUfguuuuaaau	5879	AUUUAAAACAUGUCUCCCUUAUU	7360
AD-2017661.1	uaaaacauGfUfCfucccuuauuu	4399	PadAaudAadGggagdAcAfuguuuuaaa	5880	UUUAAAACAUGUCUCCCUUAUUU	7361
AD-2017662.1	aaaacaugUfCfUfcccuuauuuu	4400	PadAaadTadAgggadGaCfauguuuuaa	5881	UUAAAACAUGUCUCCCUUAUUUA	7362
AD-2017663.1	aaacauguCfUfCfccuuauuuau	4401	PadTaadAudAagggdAgAfcauguuuua	5882	UAAAACAUGUCUCCCUUAUUUAC	7363
AD-2017664.1	aacaugucUfCfCfcuuauuuacu	4402	PadGuadAadTaaggdGaGfacauguuuu	5883	AAAACAUGUCUCCCUUAUUUACC	7364
AD-2017665.1	acaugucuCfCfCfuuauuuaccu	4403	PadGgudAadAuaagdGgAfgacauguuu	5884	AAACAUGUCUCCCUUAUUUACCA	7365
AD-2017666.1	caugucucCfCfUfuauuuaccau	4404	PadTggdTadAauaadGgGfagacauguu	5885	AACAUGUCUCCCUUAUUUACCAU	7366
AD-2017667.1	augucuccCfUfUfauuuaccauu	4405	PadAugdGudAaauadAgGfgagacaugu	5886	ACAUGUCUCCCUUAUUUACCAUA	7367
AD-2017669.1	gucucccuUfAfUfuuaccauauu	4406	PadAuadTgdGuaaadTaAfgggagacau	5887	AUGUCUCCCUUAUUUACCAUAUA	7368
AD-2017670.1	aauucugaAfAfCfacaaaauauu	4407	PadAuadTudTugugdTuUfcagaauucu	5888	AGAAUUCUGAAACACAAAAUAUG	7369
AD-2017671.1	auucugaaAfCfAfcaaaauaugu	4408	PadCaudAudTuugudGuUfucagaauuc	5889	GAAUUCUGAAACACAAAAUAUGA	7370
AD-2017672.1	caaaauauGfAfAfauaaauuggu	4409	PadCcadAudTuauudTcAfuauuuugug	5890	CACAAAAUAUGAAAUAAAAUUGGG	7371
AD-2017673.1	aaauaugaAfAfUfaaauugggau	4410	PadTccdCadAuuuadTuUfcauauuuug	5891	CAAAAUAUGAAAUAAAAUUGGGAG	7372
AD-2017674.1	auaugaaaUfAfAfauugggaguu	4411	PadAcudCcdCaauudTaUfuucauauuu	5892	AAAUAUGAAAUAAAUUGGGAGUC	7373
AD-2017675.1	uaugaaauAfAfAfuugggagucu	4412	PadGacdTcdCcaaudTuAfuuucauauu	5893	AAUAUGAAAUAAAUUGGGAGUCA	7374
AD-2017676.1	augaaauaAfAfUfugggagucau	4413	PadTgadCudCccaadTuUfauuucauau	5894	AUAUGAAAUAAAUUGGGAGUCAG	7375
AD-2017677.1	ugaaauaaAfUfUfggagucagu	4414	PadCugdAcdTcccadAuUfuauuucaua	5895	UAUGAAAUAAAUUGGGAGUCAGG	7376
AD-2017678.1	gaaauaaaUfUfGfggagucaggu	4415	PadCcudGadCucccdAaUfuuauuucau	5896	AUGAAAUAAAUUGGGAGUCAGGA	7377
AD-2017679.1	aaauaaauUfGfGfgagucaggau	4416	PadTccdTgdAcuccdCaAfuuuauuuca	5897	UGAAAUAAAUUGGGAGUCAGGAA	7378
AD-2017680.1	aauaaauuGfGfGfagucaggaau	4417	PadTucdCudGacucdCcAfauuuauuuc	5898	GAAAUAAAUUGGGAGUCAGGAAU	7379
AD-2017681.1	auaaauugGfGfAfgucaggaauu	4418	PadAuudCcdTgacudCcCfaauuuauuu	5899	AAAUAAAUUGGGAGUCAGGAAUA	7380
AD-2017682.1	uaaauuggGfAfGfucaggaauau	4419	PadTaudTcdCugacdTcCfcaauuuauu	5900	AAUAAAUUGGGAGUCAGGAAUAA	7381
AD-2017683.1	aaauugggAfGfUfcaggaauaau	4420	PadTuadTudCcugadCuCfccaauuuau	5901	AUAAAUUGGGAGUCAGGAAUAAU	7382

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017684.1	aauugggaGfUfCfaggaauaauu	4421	PadAuudAudTccugdAcUfcccaauuua	5902	UAAAUUGGGAGUCAGGAAUAAUU	7383
AD-2017685.1	auugggagUfCfAfggaauaauuu	4422	PadAaudTadTuccudGaCfucccaauuu	5903	AAAUUGGGAGUCAGGAAUAAUUA	7384
AD-2017686.1	uugggaguCfAfGfggaauaauau	4423	PadTaadTudAuuccdTgAfcucccaauu	5904	AAUUGGGAGUCAGGAAUAAUUAU	7385
AD-2017687.1	ugggagucAfGfGfaauaauuau	4424	PadAuadAudTauucdCuGfacucccaau	5905	AUUGGGAGUCAGGAAUAAUUAUU	7386
AD-2017688.1	gggagucaGfGfAfauaauuauu	4425	PadAaudAadTuauudCcUfgacucccaa	5906	UUGGGAGUCAGGAAUAAUUAUUU	7387
AD-2017689.1	ggagucagGfAfAfuaauuauuu	4426	PadAaadTadAuuaudTcCfugacuccca	5907	UGGGAGUCAGGAAUAAUUAUUUG	7388
AD-2017690.1	gagucaggAfAfUfaauuauuugu	4427	PadCaadAudAauuadTuCfcugacuccc	5908	GGGAGUCAGGAAUAAUUAUUUGU	7389
AD-2017691.1	agucaggaAfUfAfauuauuuguu	4428	PadAcadAadTaauudAuUfccugacucc	5909	GGAGUCAGGAAUAAUUAUUUGUG	7390
AD-2017692.1	gucaggaaUfAfAfuuauuugugu	4429	PadCacdAadAuaaudTaUfuccugacuc	5910	GAGUCAGGAAUAAUUAUUUGUGC	7391
AD-2017693.1	gcacuaaaUfUfUfcaauuauacu	4430	PadGuadTadAuugadAaUfuuagugcac	5911	GUGCACUAAAUUUCAAUUAUACU	7392
AD-2017694.1	caauuaaaAfGfAfaacuauccau	4431	PadTggdAudAguuudCuUfuuaauugau	5912	AUCAAUUAAAAGAAACUAUCCAC	7393
AD-2017695.1	aauuaaaaGfAfAfacuauccacu	4432	PadGugdGadTaguudTcUfuuuaauuga	5913	UCAAUUAAAAGAAACUAUCCACA	7394
AD-2017696.1	auuaaaagAfAfAfcuauccacau	4433	PadTgudGgdAuagudTuCfuuuuaauug	5914	CAAUUAAAAGAAACUAUCCACAA	7395
AD-2017697.1	uuaaaagaAfAfCfuauccacaau	4434	PadTugdTgdGauagdTuUfcuuuuaauu	5915	AAUUAAAAGAAACUAUCCACAAC	7396
AD-2017698.1	uaaaagaaAfCfUfauccacaacu	4435	PadGuudGudGgauadGuUfucuuuuaau	5916	AUUAAAAGAAACUAUCCACAACC	7397
AD-2017699.1	aaaagaaaCfUfAfuccacaaccu	4436	PadGgudTgdTggaudAgUfuucuuuuaa	5917	UUAAAAGAAACUAUCCACAACCU	7398
AD-2017700.1	aaagaaacUfAfUfccacaaccuu	4437	PadAggdTudGuggadTaGfuuucuuuua	5918	UAAAAGAAACUAUCCACAACCUG	7399
AD-2017701.1	aagaaacuAfUfCfcacaaccugu	4438	PadCagdGudTguggdAuAfguuucuuuu	5919	AAAAGAAACUAUCCACAACCUGU	7400
AD-2017702.1	agaaacuaUfCfCfacaaccuguu	4439	PadAcadGgdTugugdGaUfaguuucuuu	5920	AAAGAAACUAUCCACAACCUGUU	7401
AD-2017703.1	gaaacuauCfCfAfcaaccuguuu	4440	PadAacdAgdGuugudGgAfuaguuucuu	5921	AAGAAACUAUCCACAACCUGUUA	7402
AD-2017704.1	aaacuaucCfAfCfaaccuguuau	4441	PadTaadCadGguugdTgGfauaguuucu	5922	AGAAACUAUCCACAACCUGUUAA	7403
AD-2017705.1	aacuauccAfCfAfaccuguuaau	4442	PadTuadAcdAgguudGuGfgauaguuuc	5923	GAAACUAUCCACAACCUGUUAAU	7404
AD-2017706.1	acuauccaCfAfAfccuguuaauu	4443	PadAuudAadCaggudTgUfggauaguuu	5924	AAACUAUCCACAACCUGUUAAUG	7405
AD-2017707.1	cuauccacAfAfCfcuguuaaugu	4444	PadCaudTadAcaggdTuGfuggauaguu	5925	AACUAUCCACAACCUGUUAAUGA	7406

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO:	Antisense Sequence 5' to 3'	SEQ ID NO:	mRNA Target Sequence 5' to 3'	SEQ ID NO:
AD-2017708.1	uauccacaAfCfCfuguuaaugau	4445	PadTcadTudAacagdGuUfguggauagu	5926	ACUAUCCACAACCUGUUAAUGAA	7407
AD-2017709.1	auccacaaCfCfUfguuaaugaau	4446	PadTucdAudTaacadGgUfuguggauag	5927	CUAUCCACAACCUGUUAAUGAAA	7408
AD-2017710.1	uccacaacCfUfGfuuaaugaaau	4447	PadTuudCadTuaacdAgGfuuguggaua	5928	UAUCCACAACCUGUUAAUGAAAC	7409
AD-2017711.1	ccacaaccUfGfUfuaaugaaacu	4448	PadGuudTcdAuuaadCaGfguuguggau	5929	AUCCACAACCUGUUAAUGAAACU	7410
AD-2017712.1	cacaaccuGfUfUfaaugaaacuu	4449	PadAgudTudCauuadAcAfgguugugga	5930	UCCACAACCUGUUAAUGAAACUA	7411
AD-2017713.1	acaaccugUfUfAfaugaaacuau	4450	PadTagdTudTcauudAaCfagguugugg	5931	CCACAACCUGUUAAUGAAACUAA	7412
AD-2017714.1	caaccuguUfAfAfugaaacuaau	4451	PadTuadGudTucaudTaAfcagguugug	5932	CACAACCUGUUAAUGAAACUAAA	7413
AD-2017715.1	aaccuguuAfAfUfgaaacuaaau	4452	PadTuudAgdTuucadTuAfacagguugu	5933	ACAACCUGUUAAUGAAACUAAAA	7414
AD-2017716.1	accuguuaAfUfGfaaacuaaaau	4453	PadTuudTadGuuucdAuUfaacagguug	5934	CAACCUGUUAAUGAAACUAAAAA	7415
AD-2017717.1	ccuguuaaUfGfAfaacuaaaaau	4454	PadTuudTudAguuudCaUfuaacagguu	5935	AACCUGUUAAUGAAACUAAAAAC	7416
AD-2017718.1	cuguuaauGfAfAfacuaaaaacu	4455	PadGuudTudTaguudTcAfuuaacaggu	5936	ACCUGUUAAUGAAACUAAAAACU	7417
AD-2017719.1	uguuaaugAfAfAfcuaaaaacuu	4456	PadAgudTudTuagudTuCfauuaacagg	5937	CCUGUUAAUGAAACUAAAAACUA	7418
AD-2017722.1	gguuuaugAfUfCfaucuuaaaau	4457	PadTuudTadAgaugdAuCfauaaacccg	5938	CGGGUUUAUGAUCAUCUUAAAAU	7419
AD-2017723.1	guuuaugaUfCfAfucuuaaaauu	4458	PadAuudTudAagaudGaUfcauaaaccc	5939	GGGUUUAUGAUCAUCUUAAAAUG	7420
AD-2017725.1	aaucauauUfUfUfgagauaguau	4459	PadTacdTadTcucadAaAfuaugauuuc	5940	GAAAUCAUAUUUUGAGAUAGUAG	7421
AD-2017726.1	aucauauuUfUfGfagauaguagu	4460	PadCuadCudAucucdAaAfauaugauuu	5941	AAAUCAUAUUUUGAGAUAGUAGC	7422
AD-2017727.1	uuuaaaccAfUfUfuugaaauauu	4461	PadAuadTudTcaaadAuGfguuuaaagc	5942	GCUUUAAACCAUUUUGAAAUAUG	7423
AD-2017728.1	aaauauguUfGfAfuuuuuccau	4462	PadTggdAadAaaaudCaAfcauauuuca	5943	UGAAAUAUGUUGAUUUUUUCCAG	7424
AD-2017730.1	auauguugAfUfUfuuuuccaggu	4463	PadCcudGgdAaaaadAuCfaacauauuu	5944	AAAUAUGUUGAUUUUUUCCAGGU	7425
AD-2017731.1	uauguugaUfUfUfuuuccagguu	4464	PadAccdTgdGaaaadAaUfcaacauauu	5945	AAUAUGUUGAUUUUUUCCAGGUA	7426
AD-2017732.1	auguugauUfUfUfuuccagguau	4465	PadTacdCudGgaaadAaAfucaacauau	5946	AUAUGUUGAUUUUUUCCAGGUAA	7427
AD-2017733.1	uguugauuUfUfUfuccagguaau	4466	PadTuadCcdTggaadAaAfaucaacaua	5947	UAUGUUGAUUUUUUCCAGGUAAU	7428
AD-2017734.1	guugauuuUfUfUfccagguaauu	4467	PadAuudAcdCuggadAaAfaaucaacau	5948	AUGUUGAUUUUUUCCAGGUAAUU	7429

Table 4. Human GRB14 Unmodified Sense and Antisense Sequences Designed for VP Modification

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2122976.1	AAUUAUAUGCA UCCAUAUCAA	7430	1218-1238	UUGAUAUGGAUG CAUAUAAUUCU	7698	1216-1238
AD-2122977.1	AAUUAUAUGCA UCCAUAUCAA	7431	1218-1238	UTGATATGGAUG CAUAUAAUUCU	7699	1216-1238
AD-2122978.1	AAUUAUAUGCA UCCAUAUCAA	7432	1218-1238	UUGATATGGAUG CAUAUAAUUCU	7700	1216-1238
AD-2122979.1	CUAUGAGAAGU AUAUCAGAGA	7433	1273-1293	UCUCUGAUAUAC UUCUCAUAGGU	7701	1271-1293
AD-2122980.1	CUAUGAGAAGU AUAUCAGAGA	7434	1273-1293	UCUCTGAUAUAC UUCUCAUAGGU	7702	1271-1293
AD-2122981.1	UAUGAGAAGUA UAUCAGAGAA	7435	1274-1294	UUCUCUGAUAUA CUUCUCAUAGG	7703	1272-1294
AD-2122982.1	UAUGAGAAGUA UAUCAGAGAA	7436	1274-1294	UTCUCUGAUAUA CUUCUCAUAGG	7704	1272-1294
AD-2122983.1	UAUGAGAAGUA UAUUAGAGAA	7437	1274-1294	UUCUCUAAUAUA CUUCUCAUAGG	7705	1272-1294
AD-2122984.1	CAGGCCAGAAA AGCAGAGUUA	7438	1318-1338	UAACUCUGCUUU UCUGGCCUGAG	7706	1316-1338
AD-2122985.1	CAGGCCAGAAA AGCAGAGUUA	7439	1318-1338	UAACTCTGCUUT UCUGGCCUGAG	7707	1316-1338
AD-2122986.1	AGGCCAGAAAA GCAGAGUUAA	7440	1319-1339	UUAACUCUGCUU UUCUGGCCUGA	7708	1317-1339
AD-2122987.1	AGGCCAGAAAA GCAGAGUUAA	7441	1319-1339	UTAACUCUGCUT UUCUGGCCUGA	7709	1317-1339
AD-2122988.1	CCAGAAAAGCA GAGUUAUAGA	7442	1322-1342	UCUAUAACUCUG CUUUUCUGGCC	7710	1320-1342
AD-2122989.1	CCAGAAAAGCA GAGUUAUAGA	7443	1322-1342	UCUATAACUCUG CUUUUCUGGCC	7711	1320-1342
AD-2122990.1	GAAAAGCAGAG UUAUAGAAAA	7444	1325-1345	UUUUCUAUAACU CUGCUUUUCUG	7712	1323-1345
AD-2122991.1	GAAAAGCAGAG UUAUAGAAAA	7445	1325-1345	UTUUCUAUAACT CUGCUUUUCUG	7713	1323-1345
AD-2122992.1	AAAGCAGAGUU AUAGAAAAUA	7446	1327-1347	UAUUUUCUAUAA CUCUGCUUUUC	7714	1325-1347
AD-2122993.1	AAAGCAGAGUU AUAGAAAAUA	7447	1327-1347	UAUUTUCUAUAA CUCUGCUUUUC	7715	1325-1347
AD-2122994.1	UAUAGAAAAUC CCACUGAAGA	7448	1337-1357	UCUUCAGUGGGA UUUUCUAUAAC	7716	1335-1357
AD-2122995.1	UAUAGAAAAUC CCACUGAAGA	7449	1337-1357	UCUUCAGUGGGA UUUUCUAUAAC	7717	1335-1357
AD-2122996.1	GACUCGCUUGG AGGAAAAAAA	7450	1381-1401	UUUUUUUCCUCC AAGCGAGUCCU	7718	1379-1401
AD-2122997.1	GACUCGCUUGG AGGAAAAAAA	7451	1381-1401	UTUUTUTCCUCCA AGCGAGUCCU	7719	1379-1401
AD-2122998.1	GACUCGCUUGG AGGAAAAAAA	7452	1381-1401	UUUUTUTCCUCC AAGCGAGUCCU	7720	1379-1401

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2122999.1	GCUUGGAGGAA AAAAGGAUGA	7453	1386-1406	UCAUCCUUUUUU CCUCCAAGCGA	7721	1384-1406
AD-2123000.1	GCUUGGAGGAA AAAAGGAUGA	7454	1386-1406	UCAUCCTUUUUT CCUCCAAGCGA	7722	1384-1406
AD-2123001.1	GCUUGGAGGAA AAAAGGAUGA	7455	1386-1406	UCAUCCTUUUUU CCUCCAAGCGA	7723	1384-1406
AD-2123002.1	UUGGAGGAAAA AAGGAUGUUA	7456	1388-1408	UAACAUCCUUUU UUCCUCCAAGC	7724	1386-1408
AD-2123003.1	UUGGAGGAAAA AAGGAUGUUA	7457	1388-1408	UAACAUCCUUUT UUCCUCCAAGC	7725	1386-1408
AD-2123004.1	UUGGAGGAAAA AAGUAUGUUA	7458	1388-1408	UAACAUACUUUU UUCCUCCAAGC	7726	1386-1408
AD-2123005.1	UGGAGGAAAAA AGGAUGUUUA	7459	1389-1409	UAAACAUCCUUU UUUCCUCCAAG	7727	1387-1409
AD-2123006.1	UGGAGGAAAAA AGGAUGUUUA	7460	1389-1409	UAAACATCCUUT UUUCCUCCAAG	7728	1387-1409
AD-2123007.1	UGGAGGAAAAA AGGAUGUUUA	7461	1389-1409	UAAACATCCUUU UUUCCUCCAAG	7729	1387-1409
AD-2123008.1	AGGAAAAAAGG AUGUUUACGA	7462	1392-1412	UCGUAAACAUCC UUUUUUCCUCC	7730	1390-1412
AD-2123009.1	AGGAAAAAAGG AUGUUUACGA	7463	1392-1412	UCGUAAACAUCC UUUUUUCCUCC	7731	1390-1412
AD-2123010.1	GGAAAAAAGGA UGUUUACGCA	7464	1393-1413	UGCGUAAACAUC CUUUUUUCCUC	7732	1391-1413
AD-2123011.1	GGAAAAAAGGA UGUUUACGCA	7465	1393-1413	UGCGTAAACAUC CUUUUUUCCUC	7733	1391-1413
AD-2123012.1	GAAAAAAGGAU GUUUACGCCA	7466	1394-1414	UGGCGUAAACAU CCUUUUUUCCU	7734	1392-1414
AD-2123013.1	GAAAAAAGGAU GUUUACGCCA	7467	1394-1414	UGGCGUAAACAT CCUUUUUUCCU	7735	1392-1414
AD-2123014.1	AAAAAGGAUGU UUACGCCUGA	7468	1396-1416	UCAGGCGUAAAC AUCCUUUUUUC	7736	1394-1416
AD-2123016.1	UGGUUUCACCA CAAAAUUUCA	7469	1488-1508	UGAAAUUUUGUG GUGAAACCAUG	7737	1486-1508
AD-2123017.1	UGGUUUCACCA CAAAAUUUCA	7470	1488-1508	UGAAAUTUUGUG GUGAAACCAUG	7738	1486-1508
AD-2123018.1	GGUUUCACCAC AAAAUUUCUA	7471	1489-1509	UAGAAAUUUUGU GGUGAAACCAU	7739	1487-1509
AD-2123019.1	GGUUUCACCAC AAAAUUUCUA	7472	1489-1509	UAGAAATUUUGT GGUGAAACCAU	7740	1487-1509
AD-2123020.1	UUUCACCACAA AAUUUCUAGA	7473	1491-1511	UCUAGAAAUUUU GUGGUGAAACC	7741	1489-1511
AD-2123021.1	UUUCACCACAA AAUUUCUAGA	7474	1491-1511	UCUAGAAAUUUT GUGGUGAAACC	7742	1489-1511
AD-2123022.1	CAAAACUUUCG UACUGUCAAA	7475	1589-1609	UUUGACAGUACG AAAGUUUUGGG	7743	1587-1609
AD-2123023.1	CAAAACUUUCG UACUGUCAAA	7476	1589-1609	UTUGACAGUACG AAAGUUUUGGG	7744	1587-1609

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123024.1	CAAAACUUUCG UACUGUCAAA	7477	1589-1609	UUUGACAGUACG AAAGUUUUGGG	7745	1587-1609
AD-2123025.1	UCGUACUGUCA AUGAGUCAUA	7478	1597-1617	UAUGACUCAUUG ACAGUACGAAA	7746	1595-1617
AD-2123026.1	UCGUACUGUCA AUGAGUCAUA	7479	1597-1617	UAUGACTCAUUG ACAGUACGAAA	7747	1595-1617
AD-2123027.1	CCAGUAGAAGA UGACGGUGAA	7480	1647-1667	UUCACCGUCAUC UUCUACUGGUA	7748	1645-1667
AD-2123028.1	CCAGUAGAAGA UGACGGUGAA	7481	1647-1667	UTCACCGUCAUC UUCUACUGGUA	7749	1645-1667
AD-2123029.1	AGAAGAUGACG GUGAAAUGUA	7482	1652-1672	UACAUUUCACCG UCAUCUUCUAC	7750	1650-1672
AD-2123030.1	AGAAGAUGACG GUGAAAUGUA	7483	1652-1672	UACATUTCACCG UCAUCUUCUAC	7751	1650-1672
AD-2123031.1	GAAGAUGACGG UGAAAUGUUA	7484	1653-1673	UAACAUUUCACC GUCAUCUUCUA	7752	1651-1673
AD-2123032.1	GAAGAUGACGG UGAAAUGUUA	7485	1653-1673	UAACAUTUCACC GUCAUCUUCUA	7753	1651-1673
AD-2123033.1	UAUCAACUCAA UAAGGGCGUA	7486	1731-1751	UACGCCCUUAUU GAGUUGAUAGA	7754	1729-1751
AD-2123034.1	UAUCAACUCAA UAAGGGCGUA	7487	1731-1751	UACGCCCUUAUT GAGUUGAUAGA	7755	1729-1751
AD-2123035.1	UCAACUCAAUA AGGGCGUUCA	7488	1733-1753	UGAACGCCCUUA UUGAGUUGAUA	7756	1731-1753
AD-2123036.1	UCAACUCAAUA AGGGCGUUCA	7489	1733-1753	UGAACGCCCUUA UUGAGUUGAUA	7757	1731-1753
AD-2123037.1	AAGGGCGUUCU UCCUUGCAAA	7490	1743-1763	UUUGCAAGGAAG AACGCCCUUAU	7758	1741-1763
AD-2123038.1	AAGGGCGUUCU UCCUUGCAAA	7491	1743-1763	UTUGCAAGGAAG AACGCCCUUAU	7759	1741-1763
AD-2123039.1	UUCUUCCUUGC AAGUUGAAAA	7492	1750-1770	UUUUCAACUUGC AAGGAAGAACG	7760	1748-1770
AD-2123040.1	UUCUUCCUUGC AAGUUGAAAA	7493	1750-1770	UTUUCAACUUGC AAGGAAGAACG	7761	1748-1770
AD-2123041.1	UUCUUCCUUGC AAGUUGAAAA	7494	1750-1770	UUUUCAACUUGC AAGGAAGAACG	7762	1748-1770
AD-2123042.1	UCUUCCUUGCA AGUUGAAACA	7495	1751-1771	UGUUUCAACUUG CAAGGAAGAAC	7763	1749-1771
AD-2123043.1	UCUUCCUUGCA AGUUGAAACA	7496	1751-1771	UGUUTCAACUUG CAAGGAAGAAC	7764	1749-1771
AD-2123044.1	UCUUCCUUGCA AGUUGAAACA	7497	1751-1771	UGUUTCAACUUG CAAGGAAGAAC	7765	1749-1771
AD-2123045.1	UUCCUUGCAAG UUGAAACAUA	7498	1753-1773	UAUGUUUCAACU UGCAAGGAAGA	7766	1751-1773
AD-2123046.1	UUCCUUGCAAG UUGAAACAUA	7499	1753-1773	UAUGTUTCAACT UGCAAGGAAGA	7767	1751-1773
AD-2123047.1	UUCCUUGCAAG UUGAAACAUA	7500	1753-1773	UAUGTUTCAACU UGCAAGGAAGA	7768	1751-1773

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123048.1	UCCUUGCAAGU UGAAACAUUA	7501	1754-1774	UAAUGUUUCAAC UUGCAAGGAAG	7769	1752-1774
AD-2123049.1	UCCUUGCAAGU UGAAACAUUA	7502	1754-1774	UAAUGUTUCAAC UUGCAAGGAAG	7770	1752-1774
AD-2123050.1	UCCUUGCAAGU UGAAACAUUA	7503	1754-1774	UAAUGUTUCAAC UUGCAAGGAAG	7771	1752-1774
AD-2123051.1	CUUGCAAGUUG AAACAUUAUA	7504	1756-1776	UAUAAUGUUUCA ACUUGCAAGGA	7772	1754-1776
AD-2123052.1	CUUGCAAGUUG AAACAUUAUA	7505	1756-1776	UAUAAUGUUUCA ACUUGCAAGGA	7773	1754-1776
AD-2123053.1	UGCAAGUUGAA ACAUUAUUGA	7506	1758-1778	UCAAUAAUGUUU CAACUUGCAAG	7774	1756-1778
AD-2123054.1	UGCAAGUUGAA ACAUUAUUGA	7507	1758-1778	UCAATAAUGUUT CAACUUGCAAG	7775	1756-1778
AD-2123055.1	AGUUGAAACAU UAUUGUGCUA	7508	1762-1782	UAGCACAAUAAU GUUUCAACUUG	7776	1760-1782
AD-2123056.1	AGUUGAAACAU UAUUGUGCUA	7509	1762-1782	UAGCACAAUAAT GUUUCAACUUG	7777	1760-1782
AD-2123057.1	UUGAAACAUUA UUGUGCUAGA	7510	1764-1784	UCUAGCACAAUA AUGUUUCAACU	7778	1762-1784
AD-2123058.1	UUGAAACAUUA UUGUGCUAGA	7511	1764-1784	UCUAGCACAAUA AUGUUUCAACU	7779	1762-1784
AD-2123059.1	CAUUAUUGUGC UAGGAUUGCA	7512	1770-1790	UGCAAUCCUAGC ACAAUAAUGUU	7780	1768-1790
AD-2123060.1	CAUUAUUGUGC UAGGAUUGCA	7513	1770-1790	UGCAAUCCUAGC ACAAUAAUGUU	7781	1768-1790
AD-2123061.1	UUAUUGUGCUA GGAUUGCUCA	7514	1772-1792	UGAGCAAUCCUA GCACAAUAAUG	7782	1770-1792
AD-2123062.1	UUAUUGUGCUA GGAUUGCUCA	7515	1772-1792	UGAGCAAUCCUA GCACAAUAAUG	7783	1770-1792
AD-2123063.1	UUAUUGUGCUA GGAUUGCUCA	7516	1772-1792	UGAGCAAUCCUA GCACAAUAAUG	7784	1770-1792
AD-2123064.1	UAUUGUGCUAG GAUUGCUCUA	7517	1773-1793	UAGAGCAAUCCU AGCACAAUAAU	7785	1771-1793
AD-2123065.1	UAUUGUGCUAG GAUUGCUCUA	7518	1773-1793	UAGAGCAAUCCT AGCACAAUAAU	7786	1771-1793
AD-2123066.1	AUUGUGCUAGG AUUGCUCUCA	7519	1774-1794	UGAGAGCAAUCC UAGCACAAUAA	7787	1772-1794
AD-2123067.1	AUUGUGCUAGG AUUGCUCUCA	7520	1774-1794	UGAGAGCAAUCC UAGCACAAUAA	7788	1772-1794
AD-2123068.1	AUUGUGCUAGG AUUUCUCUCA	7521	1774-1794	UGAGAGAAAUCC UAGCACAAUAA	7789	1772-1794
AD-2123069.1	UGUGCUAGGAU UGCUCUCUAA	7522	1776-1796	UUAGAGAGCAAU CCUAGCACAAU	7790	1774-1796
AD-2123070.1	UGUGCUAGGAU UGCUCUCUAA	7523	1776-1796	UTAGAGAGCAAT CCUAGCACAAU	7791	1774-1796
AD-2123071.1	CCAGAAGUGAC UUAUUAAACA	7524	1802-1822	UGUUUAAUAAGU CACUUCUGGCU	7792	1800-1822

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123072.1	CCAGAAGUGAC UUAUUAAACA	7525	1802-1822	UGUUTAAUAAGT CACUUCUGGCU	7793	1800-1822
AD-2123073.1	CAGAAGUGACU UAUUAAACUA	7526	1803-1823	UAGUUUAAUAAG UCACUUCUGGC	7794	1801-1823
AD-2123074.1	CAGAAGUGACU UAUUAAACUA	7527	1803-1823	UAGUTUAAUAAG UCACUUCUGGC	7795	1801-1823
AD-2123075.1	GGAAAAGGACU CAAGAAAAAA	7528	1829-1849	UUUUUUCUUGAG UCCUUUUCCUU	7796	1827-1849
AD-2123076.1	GGAAAAGGACU CAAGAAAAAA	7529	1829-1849	UTUUTUCUUGAG UCCUUUUCCUU	7797	1827-1849
AD-2123077.1	AAAGGACUCAA GAAAAAUAAA	7530	1832-1852	UUUAUUUUUCUU GAGUCCUUUUC	7798	1830-1852
AD-2123078.1	AAAGGACUCAA GAAAAAUAAA	7531	1832-1852	UTUATUTUUCUT GAGUCCUUUUC	7799	1830-1852
AD-2123079.1	AAAGGACUCAA GAAAAAUAAA	7532	1832-1852	UUUATUTUUCUU GAGUCCUUUUC	7800	1830-1852
AD-2123080.1	CCAUGUGAAAA GAAUGUAUUA	7533	1883-1903	UAAUACAUUCUU UUCACAUGGUA	7801	1881-1903
AD-2123081.1	CCAUGUGAAAA GAAUGUAUUA	7534	1883-1903	UAAUACAUUCUT UUCACAUGGUA	7802	1881-1903
AD-2123082.1	CAUGUGAAAAG AAUGUAUUUA	7535	1884-1904	UAAAUACAUUCU UUUCACAUGGU	7803	1882-1904
AD-2123083.1	CAUGUGAAAAG AAUGUAUUUA	7536	1884-1904	UAAATACAUUCT UUUCACAUGGU	7804	1882-1904
AD-2123084.1	CACCUGCAAGU UACAAAAAAA	7537	1904-1924	UUUUUUUGUAAC UUGCAGGUGAA	7805	1902-1924
AD-2123085.1	CACCUGCAAGU UACAAAAAAA	7538	1904-1924	UTUUTUTGUAAC UUGCAGGUGAA	7806	1902-1924
AD-2123086.1	CACCUGCAAGU UACAAAAAAA	7539	1904-1924	UUUUTUTGUAAC UUGCAGGUGAA	7807	1902-1924
AD-2123087.1	ACCUGCAAGUU ACAAAAAAAA	7540	1905-1925	UUUUUUUUGUAA CUUGCAGGUGA	7808	1903-1925
AD-2123088.1	ACCUGCAAGUU ACAAAAAAAA	7541	1905-1925	UTUUTUTUGUAA CUUGCAGGUGA	7809	1903-1925
AD-2123089.1	AAAAAAAUAGU UUGUGCAUUA	7542	1918-1938	UAAUGCACAAAC UAUUUUUUUGU	7810	1916-1938
AD-2123090.1	AAAAAAAUAGU UUGUGCAUUA	7543	1918-1938	UAAUGCACAAAC UAUUUUUUUGU	7811	1916-1938
AD-2123091.1	UGCAAAUAAGC AAAGACUUGA	7544	1937-1957	UCAAGUCUUUGC UUAUUUGCAAU	7812	1935-1957
AD-2123092.1	UGCAAAUAAGC AAAGACUUGA	7545	1937-1957	UCAAGUCUUUGC UUAUUUGCAAU	7813	1935-1957
AD-2123093.1	CAAAUAAGCAA AGACUUGGAA	7546	1939-1959	UUCCAAGUCUUU GCUUAUUUGCA	7814	1937-1959
AD-2123094.1	CAAAUAAGCAA AGACUUGGAA	7547	1939-1959	UTCCAAGUCUUT GCUUAUUUGCA	7815	1937-1959
AD-2123095.1	CAAAUAAGCAA AGAUUUGGAA	7548	1939-1959	UUCCAAAUCUUU GCUUAUUUGCA	7816	1937-1959

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123096.1	AAAUAAGCAAA GACUUGGAUA	7549	1940-1960	UAUCCAAGUCUU UGCUUAUUUGC	7817	1938-1960
AD-2123097.1	AAAUAAGCAAA GACUUGGAUA	7550	1940-1960	UAUCCAAGUCUT UGCUUAUUUGC	7818	1938-1960
AD-2123098.1	AAAUAAGCAAA GACUUGGAUA	7551	1940-1960	UAUCCAAGUCUU UGCUUAUUUGC	7819	1938-1960
AD-2123099.1	AUAAGCAAAGA CUUGGAUUGA	7552	1942-1962	UCAAUCCAAGUC UUUGCUUAUUU	7820	1940-1962
AD-2123100.1	AUAAGCAAAGA CUUGGAUUGA	7553	1942-1962	UCAATCCAAGUC UUUGCUUAUUU	7821	1940-1962
AD-2123101.1	AAGCAAAGACU UGGAUUGACA	7554	1944-1964	UGUCAAUCCAAG UCUUUGCUUAU	7822	1942-1964
AD-2123102.1	AAGCAAAGACU UGGAUUGACA	7555	1944-1964	UGUCAATCCAAG UCUUUGCUUAU	7823	1942-1964
AD-2123103.1	AGCAAAGACUU GGAUUGACUA	7556	1945-1965	UAGUCAAUCCAA GUCUUUGCUUA	7824	1943-1965
AD-2123104.1	AGCAAAGACUU GGAUUGACUA	7557	1945-1965	UAGUCAAUCCAA GUCUUUGCUUA	7825	1943-1965
AD-2123105.1	GCAAAGACUUG GAUUGACUUA	7558	1946-1966	UAAGUCAAUCCA AGUCUUUGCUU	7826	1944-1966
AD-2123106.1	GCAAAGACUUG GAUUGACUUA	7559	1946-1966	UAAGTCAAUCCA AGUCUUUGCUU	7827	1944-1966
AD-2123107.1	CAAAGACUUGG AUUGACUUUA	7560	1947-1967	UAAAGUCAAUCC AAGUCUUUGCU	7828	1945-1967
AD-2123108.1	CAAAGACUUGG AUUGACUUUA	7561	1947-1967	UAAAGUCAAUCC AAGUCUUUGCU	7829	1945-1967
AD-2123109.1	AAAGACUUGGA UUGACUUUAA	7562	1948-1968	UUAAAGUCAAUC CAAGUCUUUGC	7830	1946-1968
AD-2123110.1	AAAGACUUGGA UUGACUUUAA	7563	1948-1968	UTAAAGTCAAUC CAAGUCUUUGC	7831	1946-1968
AD-2123111.1	AAAGACUUGGA UUGACUUUAA	7564	1948-1968	UUAAAGTCAAUC CAAGUCUUUGC	7832	1946-1968
AD-2123112.1	AAGACUUGGAU UGACUUUACA	7565	1949-1969	UGUAAAGUCAAU CCAAGUCUUUG	7833	1947-1969
AD-2123113.1	AAGACUUGGAU UGACUUUACA	7566	1949-1969	UGUAAAGUCAAT CCAAGUCUUUG	7834	1947-1969
AD-2123114.1	AAGACUUGGAU UGAUUUUACA	7567	1949-1969	UGUAAAAUCAAU CCAAGUCUUUG	7835	1947-1969
AD-2123115.1	AGACUUGGAUU GACUUUACAA	7568	1950-1970	UUGUAAAGUCAA UCCAAGUCUUU	7836	1948-1970
AD-2123116.1	AGACUUGGAUU GACUUUACAA	7569	1950-1970	UTGUAAAGUCAA UCCAAGUCUUU	7837	1948-1970
AD-2123117.1	AGACUUGGAUU GACUUUACAA	7570	1950-1970	UUGUAAAGUCAA UCCAAGUCUUU	7838	1948-1970
AD-2123118.1	GACUUGGAUUG ACUUUACAUA	7571	1951-1971	UAUGUAAAGUCA AUCCAAGUCUU	7839	1949-1971
AD-2123119.1	GACUUGGAUUG ACUUUACAUA	7572	1951-1971	UAUGTAAAGUCA AUCCAAGUCUU	7840	1949-1971

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123120.1	ACUUGGAUUGA CUUUACAUUA	7573	1952-1972	UAAUGUAAAGUC AAUCCAAGUCU	7841	1950-1972
AD-2123121.1	ACUUGGAUUGA CUUUACAUUA	7574	1952-1972	UAAUGUAAAGUC AAUCCAAGUCU	7842	1950-1972
AD-2123122.1	CUUGGAUUGAC UUUACAUUCA	7575	1953-1973	UGAAUGUAAAGU CAAUCCAAGUC	7843	1951-1973
AD-2123123.1	CUUGGAUUGAC UUUACAUUCA	7576	1953-1973	UGAATGTAAAGT CAAUCCAAGUC	7844	1951-1973
AD-2123124.1	CUUGGAUUGAC UUUACAUUCA	7577	1953-1973	UGAATGTAAAGU CAAUCCAAGUC	7845	1951-1973
AD-2123125.1	UUGGAUUGACU UUACAUUCAA	7578	1954-1974	UUGAAUGUAAAG UCAAUCCAAGU	7846	1952-1974
AD-2123126.1	UUGGAUUGACU UUACAUUCAA	7579	1954-1974	UTGAAUGUAAAG UCAAUCCAAGU	7847	1952-1974
AD-2123127.1	UUGGAUUGACU UUAUAUUCAA	7580	1954-1974	UUGAAUAUAAAG UCAAUCCAAGU	7848	1952-1974
AD-2123128.1	GAUUGACUUUA CAUUCAUCAA	7581	1957-1977	UUGAUGAAUGUA AAGUCAAUCCA	7849	1955-1977
AD-2123129.1	GAUUGACUUUA CAUUCAUCAA	7582	1957-1977	UTGATGAAUGUA AAGUCAAUCCA	7850	1955-1977
AD-2123130.1	GAUUGACUUUA CAUUCAUCAA	7583	1957-1977	UUGATGAAUGUA AAGUCAAUCCA	7851	1955-1977
AD-2123131.1	AUUGACUUUAC AUUCAUCAUA	7584	1958-1978	UAUGAUGAAUGU AAAGUCAAUCC	7852	1956-1978
AD-2123132.1	AUUGACUUUAC AUUCAUCAUA	7585	1958-1978	UAUGAUGAAUGT AAAGUCAAUCC	7853	1956-1978
AD-2123133.1	AUUGACUUUAC AUUUAUCAUA	7586	1958-1978	UAUGAUAAAUGU AAAGUCAAUCC	7854	1956-1978
AD-2123134.1	UUGACUUUACA UUCAUCAUUA	7587	1959-1979	UAAUGAUGAAUG UAAAGUCAAUC	7855	1957-1979
AD-2123135.1	UUGACUUUACA UUCAUCAUUA	7588	1959-1979	UAAUGATGAAUG UAAAGUCAAUC	7856	1957-1979
AD-2123136.1	UUGACUUUACA UUCAUCAUUA	7589	1959-1979	UAAUGATGAAUG UAAAGUCAAUC	7857	1957-1979
AD-2123137.1	CAUAUCCUGAA AUUCAUGGUA	7590	871-891	UACCAUGAAUUU CAGGAUAUGUG	7858	869-891
AD-2123138.1	CAUAUCCUGAA AUUCAUGGUA	7591	871-891	UACCAUGAAUUT CAGGAUAUGUG	7859	869-891
AD-2123139.1	AUAUCCUGAAA UUCAUGGUUA	7592	872-892	UAACCAUGAAUU UCAGGAUAUGU	7860	870-892
AD-2123140.1	AUAUCCUGAAA UUCAUGGUUA	7593	872-892	UAACCATGAAUT UCAGGAUAUGU	7861	870-892
AD-2123141.1	UAUCCUGAAAU UCAUGGUUUA	7594	873-893	UAAACCAUGAAU UUCAGGAUAUG	7862	871-893
AD-2123142.1	UAUCCUGAAAU UCAUGGUUUA	7595	873-893	UAAACCAUGAAT UUCAGGAUAUG	7863	871-893
AD-2123143.1	UAUCCUGAAAU UCAUGGUUUA	7596	873-893	UAAACCAUGAAU UUCAGGAUAUG	7864	871-893

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123144.1	AAUACAGCUGG UGGAGUUCUA	7597	1712-1732	UAGAACUCCACC AGCUGUAUUAG	7865	1710-1732
AD-2123145.1	AAUACAGCUGG UGGAGUUCUA	7598	1712-1732	UAGAACTCCACC AGCUGUAUUAG	7866	1710-1732
AD-2123146.1	AAUACAGCUGG UGGAGUUCUA	7599	1712-1732	UAGAACTCCACC AGCUGUAUUAG	7867	1710-1732
AD-2123147.1	ACAGCUGGUGG AGUUCUAUCA	7600	1715-1735	UGAUAGAACUCC ACCAGCUGUAU	7868	1713-1735
AD-2123148.1	ACAGCUGGUGG AGUUCUAUCA	7601	1715-1735	UGAUAGAACUCC ACCAGCUGUAU	7869	1713-1735
AD-2123149.1	ACAGCUGGUGG AGUUCUAUCA	7602	1715-1735	UGAUAGAACUCC ACCAGCUGUAU	7870	1713-1735
AD-2123150.1	AAGGAAAAGGA CUCAAGAAAA	7603	1827-1847	UUUUCUUGAGUC CUUUUCCUUCA	7871	1825-1847
AD-2123151.1	AAGGAAAAGGA CUCAAGAAAA	7604	1827-1847	UTUUCUTGAGUC CUUUUCCUUCA	7872	1825-1847
AD-2123152.1	AAGGAAAAGGA CUCAAGAAAA	7605	1827-1847	UUUUCUTGAGUC CUUUUCCUUCA	7873	1825-1847
AD-2123153.1	AUUUCACCUGC AAGUUACAAA	7606	1900-1920	UUUGUAACUUGC AGGUGAAAUAC	7874	1898-1920
AD-2123154.1	AUUUCACCUGC AAGUUACAAA	7607	1900-1920	UTUGTAACUUGC AGGUGAAAUAC	7875	1898-1920
AD-2123155.1	AUUUCACCUGC AAGUUACAAA	7608	1900-1920	UUUGTAACUUGC AGGUGAAAUAC	7876	1898-1920
AD-2123156.1	UUAUGCCAAAU AUGAGUUCUA	7609	743-763	UAGAACUCAUAU UUGGCAUAAUU	7877	741-763
AD-2123157.1	UUAUGCCAAAU AUGAGUUCUA	7610	743-763	UAGAACTCAUAT UUGGCAUAAUU	7878	741-763
AD-2123158.1	CAAAUAUGAGU UCUUUAAAAA	7611	749-769	UUUUUAAAGAAC UCAUAUUUGGC	7879	747-769
AD-2123159.1	CAAAUAUGAGU UCUUUAAAAA	7612	749-769	UTUUTAAAGAAC UCAUAUUUGGC	7880	747-769
AD-2123160.1	CCAGAGCAUAU GGUAUCUUUA	7613	786-806	UAAAGAUACCAU AUGCUCUGGAA	7881	784-806
AD-2123161.1	CCAGAGCAUAU GGUAUCUUUA	7614	786-806	UAAAGATACCAT AUGCUCUGGAA	7882	784-806
AD-2123162.1	AGAGCAUAUGG UAUCUUUUGA	7615	788-808	UCAAAAGAUACC AUAUGCUCUGG	7883	786-808
AD-2123163.1	AGAGCAUAUGG UAUCUUUUGA	7616	788-808	UCAAAAGAUACC AUAUGCUCUGG	7884	786-808
AD-2123164.1	GAGCAUAUGGU AUCUUUUGCA	7617	789-809	UGCAAAAGAUAC CAUAUGCUCUG	7885	787-809
AD-2123165.1	GAGCAUAUGGU AUCUUUUGCA	7618	789-809	UGCAAAAGAUAC CAUAUGCUCUG	7886	787-809
AD-2123166.1	AGCAUAUGGUA UCUUUUGCAA	7619	790-810	UUGCAAAAGAUA CCAUAUGCUCU	7887	788-810
AD-2123167.1	AGCAUAUGGUA UCUUUUGCAA	7620	790-810	UTGCAAAAGAUA CCAUAUGCUCU	7888	788-810

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123168.1	AGAUGUUUCUG AGUUCAAGCA	7621	850-870	UGCUUGAACUCA GAAACAUCUGC	7889	848-870
AD-2123169.1	AGAUGUUUCUG AGUUCAAGCA	7622	850-870	UGCUTGAACUCA GAAACAUCUGC	7890	848-870
AD-2123170.1	AGAUGUUUCUG AGUUCAAGCA	7623	850-870	UGCUTGAACUCA GAAACAUCUGC	7891	848-870
AD-2123171.1	AUGUUUCUGAG UUCAAGCACA	7624	852-872	UGUGCUUGAACU CAGAAACAUCU	7892	850-872
AD-2123172.1	AUGUUUCUGAG UUCAAGCACA	7625	852-872	UGUGCUTGAACT CAGAAACAUCU	7893	850-872
AD-2123173.1	AUGUUUCUGAG UUCAAGCACA	7626	852-872	UGUGCUTGAACU CAGAAACAUCU	7894	850-872
AD-2123174.1	GUUUCUGAGUU CAAGCACAUA	7627	854-874	UAUGUGCUUGAA CUCAGAAACAU	7895	852-874
AD-2123175.1	GUUUCUGAGUU CAAGCACAUA	7628	854-874	UAUGTGCUUGAA CUCAGAAACAU	7896	852-874
AD-2123176.1	GUUUCUGAGUU CAAUCACAUA	7629	854-874	UAUGTGAUUGAA CUCAGAAACAU	7897	852-874
AD-2123177.1	AUCCUGAAAUU CAUGGUUUCA	7630	874-894	UGAAACCAUGAA UUUCAGGAUAU	7898	872-894
AD-2123178.1	AUCCUGAAAUU CAUGGUUUCA	7631	874-894	UGAAACCAUGAA UUUCAGGAUAU	7899	872-894
AD-2123179.1	AUCCUGAAAUU CAUUGUUUCA	7632	874-894	UGAAACAAUGAA UUUCAGGAUAU	7900	872-894
AD-2123180.1	GAAAUUCAUGG UUUCUUACAA	7633	879-899	UUGUAAGAAACC AUGAAUUUCAG	7901	877-899
AD-2123181.1	GAAAUUCAUGG UUUCUUACAA	7634	879-899	UTGUAAGAAACC AUGAAUUUCAG	7902	877-899
AD-2123182.1	GAAAUUCAUGG UUUUUUACAA	7635	879-899	UUGUAAAAAACC AUGAAUUUCAG	7903	877-899
AD-2123183.1	UUCAUGGUUUC UUACAUGCGA	7636	883-903	UCGCAUGUAAGA AACCAUGAAUU	7904	881-903
AD-2123184.1	UUCAUGGUUUC UUACAUGCGA	7637	883-903	UCGCAUGUAAGA AACCAUGAAUU	7905	881-903
AD-2123185.1	UUCAUGGUUUC UUAUAUGCGA	7638	883-903	UCGCAUAUAAGA AACCAUGAAUU	7906	881-903
AD-2123186.1	UCAUGGUUUCU UACAUGCGAA	7639	884-904	UUCGCAUGUAAG AAACCAUGAAU	7907	882-904
AD-2123187.1	UCAUGGUUUCU UACAUGCGAA	7640	884-904	UTCGCATGUAAG AAACCAUGAAU	7908	882-904
AD-2123188.1	UCAUGGUUUCU UACAUGCGAA	7641	884-904	UUCGCATGUAAG AAACCAUGAAU	7909	882-904
AD-2123189.1	AGGGAAAGAAG UCUUGGAAAA	7642	910-930	UUUUCCAAGACU UCUUUCCCUGU	7910	908-930
AD-2123190.1	AGGGAAAGAAG UCUUGGAAAA	7643	910-930	UTUUCCAAGACT UCUUUCCCUGU	7911	908-930
AD-2123191.1	AGGGAAAGAAG UCUUGGAAAA	7644	910-930	UUUUCCAAGACU UCUUUCCCUGU	7912	908-930

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123192.1	GGAAAGAAGUC UUGGAAAAAA	7645	912-932	UUUUUUCCAAGA CUUCUUUCCCU	7913	910-932
AD-2123193.1	GGAAAGAAGUC UUGGAAAAAA	7646	912-932	UTUUTUCCAAGA CUUCUUUCCCU	7914	910-932
AD-2123194.1	GGAAAGAAGUC UUGUAAAAAA	7647	912-932	UUUUTUACAAGA CUUCUUUCCCU	7915	910-932
AD-2123195.1	GAAAGAAGUCU UGGAAAAAAA	7648	913-933	UUUUUUUCCAAG ACUUCUUUCCC	7916	911-933
AD-2123196.1	GAAAGAAGUCU UGGAAAAAAA	7649	913-933	UTUUTUTCCAAG ACUUCUUUCCC	7917	911-933
AD-2123197.1	GAAAGAAGUCU UGGAAAAAAA	7650	913-933	UUUUTUTCCAAG ACUUCUUUCCC	7918	911-933
AD-2123198.1	AAAGAAGUCUU GGAAAAAAAA	7651	914-934	UUUUUUUUCCAA GACUUCUUUCC	7919	912-934
AD-2123199.1	AAAGAAGUCUU GGAAAAAAAA	7652	914-934	UTUUTUTUCCAA GACUUCUUUCC	7920	912-934
AD-2123200.1	AAGUCUUGGAA AAAAAUUUAA	7653	918-938	UUAAAUUUUUUU CCAAGACUUCU	7921	916-938
AD-2123201.1	AAGUCUUGGAA AAAAAUUUAA	7654	918-938	UTAAAUTUUUUT CCAAGACUUCU	7922	916-938
AD-2123202.1	AGUCUUGGAAA AAAAUUUACA	7655	919-939	UGUAAAUUUUUU UCCAAGACUUC	7923	917-939
AD-2123203.1	AGUCUUGGAAA AAAAUUUACA	7656	919-939	UGUAAATUUUUT UCCAAGACUUC	7924	917-939
AD-2123204.1	AACCGCGGCAU UUGCAGUUUA	7657	991-1011	UAAACUGCAAAU GCCGCGGUUCC	7925	989-1011
AD-2123205.1	AACCGCGGCAU UUGCAGUUUA	7658	991-1011	UAAACUGCAAAT GCCGCGGUUCC	7926	989-1011
AD-2123206.1	AACCGCGGCAU UUGUAGUUUA	7659	991-1011	UAAACUACAAAU GCCGCGGUUCC	7927	989-1011
AD-2123207.1	GCAUUUGCAGU UUUUCAGCGA	7660	998-1018	UCGCUGAAAAAC UGCAAAUGCCG	7928	996-1018
AD-2123208.1	GCAUUUGCAGU UUUUCAGCGA	7661	998-1018	UCGCTGAAAAAC UGCAAAUGCCG	7929	996-1018
AD-2123209.1	GCAUUUGCAGU UUUUCAGCGA	7662	998-1018	UCGCTGAAAAAC UGCAAAUGCCG	7930	996-1018
AD-2123210.1	AUUUGCAGUUU UUCAGCGAAA	7663	1000-1020	UUUCGCUGAAAA ACUGCAAAUGC	7931	998-1020
AD-2123211.1	AUUUGCAGUUU UUCAGCGAAA	7664	1000-1020	UTUCGCTGAAAA ACUGCAAAUGC	7932	998-1020
AD-2123212.1	AUUUGCAGUUU UUCAGCGAAA	7665	1000-1020	UUUCGCTGAAAA ACUGCAAAUGC	7933	998-1020
AD-2123213.1	UUGCAGUUUUU CAGCGAAUUA	7666	1002-1022	UAAUUCGCUGAA AAACUGCAAAU	7934	1000-1022
AD-2123214.1	UUGCAGUUUUU CAGCGAAUUA	7667	1002-1022	UAAUTCGCUGAA AAACUGCAAAU	7935	1000-1022
AD-2123215.1	UUGCAGUUUUU CAGUGAAUUA	7668	1002-1022	UAAUTCACUGAA AAACUGCAAAU	7936	1000-1022

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123216.1	UUUCAGCGAAU UUGGCAAUAA	7669	1010-1030	UUAUUGCCAAAU UCGCUGAAAAA	7937	1008-1030
AD-2123217.1	UUUCAGCGAAU UUGGCAAUAA	7670	1010-1030	UTAUTGCCAAAT UCGCUGAAAAA	7938	1008-1030
AD-2123218.1	UUUCAGCGAAU UUGUCAAUAA	7671	1010-1030	UUAUTGACAAAU UCGCUGAAAAA	7939	1008-1030
AD-2123219.1	GAAUUUGGCAA UAGUGAUAUA	7672	1017-1037	UAUAUCACUAUU GCCAAAUUCGC	7940	1015-1037
AD-2123220.1	GAAUUUGGCAA UAGUGAUAUA	7673	1017-1037	UAUATCACUAUT GCCAAAUUCGC	7941	1015-1037
AD-2123221.1	UGGCAAUAGUG AUAUUUAUGA	7674	1022-1042	UCAUAAAUAUCA CUAUUGCCAAA	7942	1020-1042
AD-2123222.1	UGGCAAUAGUG AUAUUUAUGA	7675	1022-1042	UCAUAAAUAUCA CUAUUGCCAAA	7943	1020-1042
AD-2123223.1	GGCAAUAGUGA UAUUUAUGUA	7676	1023-1043	UACAUAAAUAUC ACUAUUGCCAA	7944	1021-1043
AD-2123224.1	GGCAAUAGUGA UAUUUAUGUA	7677	1023-1043	UACATAAAUAUC ACUAUUGCCAA	7945	1021-1043
AD-2123225.1	GCAAUAGUGAU AUUUAUGUGA	7678	1024-1044	UCACAUAAAUAU CACUAUUGCCA	7946	1022-1044
AD-2123226.1	GCAAUAGUGAU AUUUAUGUGA	7679	1024-1044	UCACAUAAAUAT CACUAUUGCCA	7947	1022-1044
AD-2123227.1	ACAUGGAGCAC CGACUAACUA	7680	1064-1084	UAGUUAGUCGGU GCUCCAUGUUU	7948	1062-1084
AD-2123228.1	ACAUGGAGCAC CGACUAACUA	7681	1064-1084	UAGUTAGUCGGT GCUCCAUGUUU	7949	1062-1084
AD-2123229.1	ACAUGGAGCAC CGAUUAACUA	7682	1064-1084	UAGUTAAUCGGU GCUCCAUGUUU	7950	1062-1084
AD-2123230.1	CUAACUAUGGA UUCUGCUUUA	7683	1078-1098	UAAAGCAGAAUC CAUAGUUAGUC	7951	1076-1098
AD-2123231.1	CUAACUAUGGA UUCUGCUUUA	7684	1078-1098	UAAAGCAGAAUC CAUAGUUAGUC	7952	1076-1098
AD-2123232.1	CUAACUAUGGA UUCUGCUUUA	7685	1078-1098	UAAAGCAGAAUC CAUAGUUAGUC	7953	1076-1098
AD-2123233.1	UGCAGCUGUAC CAGAAUUAUA	7686	1204-1224	UAUAAUUCUGGU ACAGCUGCAUG	7954	1202-1224
AD-2123234.1	UGCAGCUGUAC CAGAAUUAUA	7687	1204-1224	UAUAAUTCUGGT ACAGCUGCAUG	7955	1202-1224
AD-2123235.1	GCUGUACCAGA AUUAUAUGCA	7688	1208-1228	UGCAUAUAAUUC UGGUACAGCUG	7956	1206-1228
AD-2123236.1	GCUGUACCAGA AUUAUAUGCA	7689	1208-1228	UGCATATAAUUC UGGUACAGCUG	7957	1206-1228
AD-2123237.1	CUGUACCAGAA UUAUAUGCAA	7690	1209-1229	UUGCAUAUAAUU CUGGUACAGCU	7958	1207-1229
AD-2123238.1	CUGUACCAGAA UUAUAUGCAA	7691	1209-1229	UTGCAUAUAAUT CUGGUACAGCU	7959	1207-1229
AD-2123239.1	CUGUACCAGAA UUAUAUGCAA	7692	1209-1229	UUGCAUAUAAUU CUGGUACAGCU	7960	1207-1229

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2123240.1	UGUACCAGAAU UAUAUGCAUA	7693	1210-1230	UAUGCAUAUAAU UCUGGUACAGC	7961	1208-1230
AD-2123241.1	UGUACCAGAAU UAUAUGCAUA	7694	1210-1230	UAUGCATAUAAT UCUGGUACAGC	7962	1208-1230
AD-2123242.1	ACCAGAAUUAU AUGCAUCCAA	7695	1213-1233	UUGGAUGCAUAU AAUUCUGGUAC	7963	1211-1233
AD-2123243.1	ACCAGAAUUAU AUGCAUCCAA	7696	1213-1233	UTGGAUGCAUAT AAUUCUGGUAC	7964	1211-1233
AD-2123244.1	ACCAGAAUUAU AUGUAUCCAA	7697	1213-1233	UUGGAUACAUAU AAUUCUGGUAC	7965	1211-1233

Table 5. Human GRB14 Modified Sense and Antisense Sequences With VP Modification

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2122976.1	asasuuauAfuGfCf AfuccauaucaaL96	7966	VPusUfsgauAfuggaug cAfuAfuaauuscsu	8234	AGAAUUAUAUGC AUCCAUAUCAA	8502
AD-2122977.1	asasuuauauGfCfA fuccauaucaaL96	7967	VPusdTsgadTadTggau dGcAfuauaauuscsu	8235	AGAAUUAUAUGC AUCCAUAUCAA	8503
AD-2122978.1	asasuuauAfuGfCf AfuccauaucaaL96	7968	VPusUfsgadTa(Tgn)g gaugcAfuAfuaauuscsu	8236	AGAAUUAUAUGC AUCCAUAUCAA	8504
AD-2122979.1	csusaugaGfaAfGf UfauaucagagaL96	7969	VPusCfsucuGfauauac uUfcUfcauagsgsu	8237	ACCUAUGAGAAG UAUAUCAGAGA	8505
AD-2122980.1	csusaugagaAfGfU fauaucagagaL96	7970	VPusdCsucdTgdAuau adCuUfcucauagsgsu	8238	ACCUAUGAGAAG UAUAUCAGAGA	8506
AD-2122981.1	usasugagAfaGfUf AfuaucagagaaL96	7971	VPusUfscucUfgauaua cUfuCfucauasgsg	8239	CCUAUGAGAAGU AUAUCAGAGAA	8507
AD-2122982.1	usasugagaaGfUfA fuaucagagaaL96	7972	VPusdTscudCudGaua udAcUfucucauasgsg	8240	CCUAUGAGAAGU AUAUCAGAGAA	8508
AD-2122983.1	usasugagAfaGfUf AfuauuagagaaL96	7973	VPusUfscudCudAaua uacUfuCfucauasgsg	8241	CCUAUGAGAAGU AUAUCAGAGAA	8509
AD-2122984.1	csasggccAfgAfAf AfagcagaguuaL96	7974	VPusAfsacuCfugcuuu uCfuGfgccugsasg	8242	CUCAGGCCAGAA AAGCAGAGUUA	8510
AD-2122985.1	csasggccagAfAfA fagcagaguuaL96	7975	VPusdAsacdTcdTgcu udTuCfuggccugsasg	8243	CUCAGGCCAGAA AAGCAGAGUUA	8511
AD-2122986.1	asgsgccaGfaAfAf Afgcagaguuaa L96	7976	VPusUfsaacUfcugcuu uUfcUfggccusgsa	8244	UCAGGCCAGAAA AGCAGAGUUAU	8512
AD-2122987.1	asgsgccagaAfAfA fgcagaguuaaL96	7977	VPusdTsaadCudCugc udTuUfcuggccusgsa	8245	UCAGGCCAGAAA AGCAGAGUUAU	8513
AD-2122988.1	cscsagaaAfaGfCf AfgaguuauagaL96	7978	VPusCfsuauAfacucug cUfuUfucuggscsc	8246	GGCCAGAAAAGC AGAGUUAUAGA	8514
AD-2122989.1	cscsagaaaaGfCfAf gaguuauagaL96	7979	VPusdCsuadTadAcuc udGcUfuuucuggscsc	8247	GGCCAGAAAAGC AGAGUUAUAGA	8515
AD-2122990.1	gsasaaagCfaGfAf GfuuauagaaaaL96	7980	VPusUfsuucUfauaacu cUfgCfuuuucsusg	8248	CAGAAAAGCAGA GUUAUAGAAAA	8516
AD-2122991.1	gsasaaagcaGfAfGf uuauagaaaaL96	7981	VPusdTsuudCudAuaa cdTcUfgcuuuucsusg	8249	CAGAAAAGCAGA GUUAUAGAAAA	8517

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2122992.1	asasagcaGfaGfUf Ufauagaaaaua L96	7982	VPusAfsuuuUfcuauaa cUfcUfgcuuususc	8250	GAAAAGCAGAGU UAUAGAAAAUC	8518
AD-2122993.1	asasagcagaGfUfUf auagaaaaua L96	7983	VPusdAsuudTudCuau adAcUfcugcuuususc	8251	GAAAAGCAGAGU UAUAGAAAAUC	8519
AD-2122994.1	usasuagaAfaAfUf Cfccacugaaga L96	7984	VPusCfsuucAfguggga uUfuUfcuauasasc	8252	GUUAUAGAAAAU CCCACUGAAGC	8520
AD-2122995.1	usasuagaaaAfUfCf ccacugaaga L96	7985	VPusdCsuudCadGugg gdAuUfuucuauasasc	8253	GUUAUAGAAAAU CCCACUGAAGC	8521
AD-2122996.1	gsascucgCfuUfGf Gfaggaaaaaaa L96	7986	VPusUfsuuuUfuccucc aAfgCfgagucscsu	8254	AGGACUCGCUUG GAGGAAAAAAG	8522
AD-2122997.1	gsascucgcuUfGfG faggaaaaaaa L96	7987	VPusdTsuudTudTccuc dCaAfgcgagucscsu	8255	AGGACUCGCUUG GAGGAAAAAAG	8523
AD-2122998.1	gsascucgCfuUfGf Gfaggaaaaaaa L96	7988	VPusUfsuudTu(Tgn)c cuccaAfgCfgagucscsu	8256	AGGACUCGCUUG GAGGAAAAAAG	8524
AD-2122999.1	gscsuuggAfgGfAf Afaaaaggauga L96	7989	VPusCfsaucCfuuuuuu cCfuCfcaagcsgsa	8257	UCGCUUGGAGGA AAAAAGGAUGU	8525
AD-2123000.1	gscsuuggagGfAfA faaaaggauga L96	7990	VPusdCsaudCcdTuuu udTcCfuccaagcsgsa	8258	UCGCUUGGAGGA AAAAAGGAUGU	8526
AD-2123001.1	gscsuuggAfgGfAf Afaaaaggauga L96	7991	VPusCfsaudCc(Tgn)u uuuucCfuCfcaagcsgsa	8259	UCGCUUGGAGGA AAAAAGGAUGU	8527
AD-2123002.1	ususggagGfaAfAf Afaaggauguua L96	7992	VPusAfsacaUfccuuuu uUfcCfuccaasgsc	8260	GCUUGGAGGAAA AAAGGAUGUUU	8528
AD-2123003.1	ususggaggaAfAfA faaggauguua L96	7993	VPusdAsacdAudCcuu udTuUfccuccaasgsc	8261	GCUUGGAGGAAA AAAGGAUGUUU	8529
AD-2123004.1	ususggagGfaAfAf Afaaguauguua L96	7994	VPusAfsacdAudAcuu uuuUfcCfuccaasgsc	8262	GCUUGGAGGAAA AAAGGAUGUUU	8530
AD-2123005.1	usgsgaggAfaAfAf Afaggauguuua L96	7995	VPusAfsaacAfuccuuu uUfuCfcuccasasg	8263	CUUGGAGGAAAA AAGGAUGUUUA	8531
AD-2123006.1	usgsgaggaaAfAfA faggauguuua L96	7996	VPusdAsaadCadTccu udTuUfuccuccasasg	8264	CUUGGAGGAAAA AAGGAUGUUUA	8532
AD-2123007.1	usgsgaggAfaAfAf Afaggauguuua L96	7997	VPusAfsaadCa(Tgn)c cuuuuUfuCfcuccasasg	8265	CUUGGAGGAAAA AAGGAUGUUUA	8533
AD-2123008.1	asgsgaaaAfaAfGf Gfauguuuacga L96	7998	VPusCfsguaAfacaucc uUfuUfuuccuscsc	8266	GGAGGAAAAAAG GAUGUUUACGC	8534
AD-2123009.1	asgsgaaaaaAfGfGf auguuuacga L96	7999	VPusdCsgudAadAcau cdCuUfuuuuccuscsc	8267	GGAGGAAAAAAG GAUGUUUACGC	8535
AD-2123010.1	gsgsaaaaAfaGfGf Afuguuuacgca L96	8000	VPusGfscguAfaacauc cUfuUfuuuccsusc	8268	GAGGAAAAAAGG AUGUUUACGCC	8536
AD-2123011.1	gsgsaaaaaaGfGfAf uguuuacgca L96	8001	VPusdGscgdTadAaca udCcUfuuuuuccsusc	8269	GAGGAAAAAAGG AUGUUUACGCC	8537
AD-2123012.1	gsasaaaaAfgGfAf Ufguuuacgcca L96	8002	VPusGfsgcgUfaaacau cCfuUfuuuucscsu	8270	AGGAAAAAAGGA UGUUUACGCCU	8538
AD-2123013.1	gsasaaaaagGfAfUf guuuacgcca L96	8003	VPusdGsgcdGudAaac adTcCfuuuuuucscsu	8271	AGGAAAAAAGGA UGUUUACGCCU	8539
AD-2123014.1	asasaaagGfaUfGf Ufuuacgccuga L96	8004	VPusCfsaggCfguaaaca UfcCfuuuuususc	8272	GAAAAAAGGAUG UUUACGCCUGG	8540
AD-2123016.1	usgsguuuCfaCfCf Afcaaaauuuca L96	8005	VPusGfsaaaUfuuugug gUfgAfaaccasusg	8273	CAUGGUUUCACC ACAAAAUUUCU	8541

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123017.1	usgsguuucaCfCfAfcaaaauuucaL96	8006	VPusdGsaadAudTuugudGgUfgaaaccasusg	8274	CAUGGUUUCACCACAAAAUUUCU	8542
AD-2123018.1	gsgsuuucAfcCfAfCfaaaauuucuaL96	8007	VPusAfsgaaAfuuuugugGfuGfaaaccsasu	8275	AUGGUUUCACCACAAAAUUUCUA	8543
AD-2123019.1	gsgsuuucacCfAfCfaaaauuucuaL96	8008	VPusdAsgadAadTuuugdTgGfugaaaccsasu	8276	AUGGUUUCACCACAAAAUUUCUA	8544
AD-2123020.1	usususcacCfaCfAfAfaauuucuagaL96	8009	VPusCfsuagAfaauuuugUfgGfugaaascsc	8277	GGUUUCACCACAAAAUUUCUAGA	8545
AD-2123021.1	usususcaccaCfAfAfAfaauuucuagaL96	8010	VPusdCsuadGadAauuudTgUfggugaaascsc	8278	GGUUUCACCACAAAAUUUCUAGA	8546
AD-2123022.1	csasaaacUfuUfCfGfuacugucaaaL96	8011	VPusUfsugaCfaguacgaAfaGfuuuugsgsg	8279	CCCAAAACUUUCGUACUGUCAAU	8547
AD-2123023.1	csasaaacuuUfCfGfuacugucaaaL96	8012	VPusdTsugdAcdAguacdGaAfaguuuugsgsg	8280	CCCAAAACUUUCGUACUGUCAAU	8548
AD-2123024.1	csasaaacUfuUfCfGfuacugucaaaL96	8013	VPusUfsugdAc(Agn)guacgaAfaGfuuuugsgsg	8281	CCCAAAACUUUCGUACUGUCAAU	8549
AD-2123025.1	uscsguacUfgUfCfAfaugagucauaL96	8014	VPusAfsugaCfucauugaCfaGfuacgasasa	8282	UUUCGUACUGUCAAUGAGUCAUG	8550
AD-2123026.1	uscsguacugUfCfAfaugagucauaL96	8015	VPusdAsugdAcdTcaudGaCfaguacgasasa	8283	UUUCGUACUGUCAAUGAGUCAUG	8551
AD-2123027.1	cscsaguaGfaAfGfAfugacggugaaL96	8016	VPusUfscacCfgucaucuUfcUfacuggsusa	8284	UACCAGUAGAAGAUGACGGUGAA	8552
AD-2123028.1	cscsaguagaAfGfAffugacggugaaL96	8017	VPusdTscadCcdGucaudCuUfcuacuggsusa	8285	UACCAGUAGAAGAUGACGGUGAA	8553
AD-2123029.1	asgsaagaUfgAfCfGfgugaaauguaL96	8018	VPusAfscauUfucaccguCfaUfcuucusasc	8286	GUAGAAGAUGACGGUGAAAUGUU	8554
AD-2123030.1	asgsaagaugAfCfGfgugaaauguaL96	8019	VPusdAscadTudTcaccdGuCfaucuucusasc	8287	GUAGAAGAUGACGGUGAAAUGUU	8555
AD-2123031.1	gsasagauGfaCfGfGfugaaauguuaL96	8020	VPusAfsacaUfuucaccgUfcAfucuucsusa	8288	UAGAAGAUGACGGUGAAAUGUUC	8556
AD-2123032.1	gsasagaugaCfGfGfugaaauguuaL96	8021	VPusdAsacdAudTucacdCgUfcaucuucsusa	8289	UAGAAGAUGACGGUGAAAUGUUC	8557
AD-2123033.1	usasucaaCfuCfAfAfuaagggcguaL96	8022	VPusAfscgcCfcuuauugAfgUfugauasgsa	8290	UCUAUCAACUCAAUAAGGGCGUU	8558
AD-2123034.1	usasucaacuCfAfAfAfuaagggcguaL96	8023	VPusdAscgdCcdCuuaudTgAfguugauasgsa	8291	UCUAUCAACUCAAUAAGGGCGUU	8559
AD-2123035.1	uscsaacuCfaAfUfAfagggcguucaL96	8024	VPusGfsaacGfcccuuauUfgAfguugasusa	8292	UAUCAACUCAAUAAGGGCGUUCU	8560
AD-2123036.1	uscsaacucaAfUfAfagggcguucaL96	8025	VPusdGsaadCgdCccuudAuUfgaguugasusa	8293	UAUCAACUCAAUAAGGGCGUUCU	8561
AD-2123037.1	asasgggcGfuUfCfUfuccuugcaaaL96	8026	VPusUfsugcAfaggaagaAfcGfcccuusasu	8294	AUAAGGGCGUUCUUCCUUGCAAG	8562
AD-2123038.1	asasgggcguUfCfUfuccuugcaaaL96	8027	VPusdTsugdCadAggaadGaAfcgcccuusasu	8295	AUAAGGGCGUUCUUCCUUGCAAG	8563
AD-2123039.1	ususcuucCfuUfGfCfaaguugaaaaL96	8028	VPusUfsuucAfacuugcaAfgGfaagaascsg	8296	CGUUCUUCCUUGCAAGUUGAAAC	8564
AD-2123040.1	ususcuuccuUfGfCfaaguugaaaaL96	8029	VPusdTsuudCadAcuugdCaAfggaagaascsg	8297	CGUUCUUCCUUGCAAGUUGAAAC	8565

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123041.1	ususcuucCfuUfGfCfaaguugaaaaL96	8030	VPusUfsuudCa(Agn)cuugcaAfgGfaagaascsg	8298	CGUUCUUCCUUGCAAGUUGAAAC	8566
AD-2123042.1	uscsuuccUfuGfCfAfaguugaaacaL96	8031	VPusGfsuuuCfaacuugcAfaGfgaagasasc	8299	GUUCUUCCUUGCAAGUUGAAACA	8567
AD-2123043.1	uscsuuccuuGfCfAfaguugaaacaL96	8032	VPusdGsuudTcdAacudGcAfaggaagasasc	8300	GUUCUUCCUUGCAAGUUGAAACA	8568
AD-2123044.1	uscsuuccUfuGfCfAfaguugaaacaL96	8033	VPusGfsuudTc(Agn)acuugcAfaGfgaagasasc	8301	GUUCUUCCUUGCAAGUUGAAACA	8569
AD-2123045.1	ususccuuGfcAfAfGfuugaaacauaL96	8034	VPusAfsuguUfucaacuuGfcAfaggaasgsa	8302	UCUUCCUUGCAAGUUGAAACAUU	8570
AD-2123046.1	ususccuugcAfAfGfuugaaacauaL96	8035	VPusdAsugdTudTcaacdTuGfcaaggaasgsa	8303	UCUUCCUUGCAAGUUGAAACAUU	8571
AD-2123047.1	ususccuuGfcAfAfGfuugaaacauaL96	8036	VPusAfsugdTu(Tgn)caacuuGfcAfaggaasgsa	8304	UCUUCCUUGCAAGUUGAAACAUU	8572
AD-2123048.1	uscscuugCfaAfGfUfugaaacauuaL96	8037	VPusAfsaugUfuucaacuUfgCfaaggasasg	8305	CUUCCUUGCAAGUUGAAACAUUA	8573
AD-2123049.1	uscscuugcaAfGfUfugaaacauuaL96	8038	VPusdAsaudGudTucaadCuUfgcaaggasasg	8306	CUUCCUUGCAAGUUGAAACAUUA	8574
AD-2123050.1	uscscuugCfaAfGfUfugaaacauuaL96	8039	VPusAfsaudGu(Tgn)ucaacuUfgCfaaggasasg	8307	CUUCCUUGCAAGUUGAAACAUUA	8575
AD-2123051.1	csusugcaAfgUfUfGfaaacauuauaL96	8040	VPusAfsuaaUfguuucaaCfuUfgcaagsgsa	8308	UCCUUGCAAGUUGAAACAUUAUU	8576
AD-2123052.1	csusugcaagUfUfGfaaacauuauaL96	8041	VPusdAsuadAudGuuucdAaCfuugcaagsgsa	8309	UCCUUGCAAGUUGAAACAUUAUU	8577
AD-2123053.1	usgscaagUfuGfAfAfacauuauugaL96	8042	VPusCfsaauAfauguuucAfaCfuugcasasg	8310	CUUGCAAGUUGAAACAUUAUUGU	8578
AD-2123054.1	usgscaaguuGfAfAfacauuauugaL96	8043	VPusdCsaadTadAugudTcAfacuugcasasg	8311	CUUGCAAGUUGAAACAUUAUUGU	8579
AD-2123055.1	asgsuugaAfaCfAfUfuauugugcuaL96	8044	VPusAfsgcaCfaauaaugUfuUfcaacususg	8312	CAAGUUGAAACAUUAUUGUGCUA	8580
AD-2123056.1	asgsuugaaaCfAfUfuauugugcuaL96	8045	VPusdAsgcdAcdAauaadTgUfuucaacususg	8313	CAAGUUGAAACAUUAUUGUGCUA	8581
AD-2123057.1	ususgaaaCfaUfUfAfuugugcuagaL96	8046	VPusCfsuagCfacaauaaUfgUfuucaascsu	8314	AGUUGAAACAUUAUUGUGCUAGG	8582
AD-2123058.1	ususgaaacaUfUfAfuugugcuagaL96	8047	VPusdCsuadGcdAcaaudAaUfguuucaascsu	8315	AGUUGAAACAUUAUUGUGCUAGG	8583
AD-2123059.1	csasuuauUfgUfGfCfuaggauugcaL96	8048	VPusGfscaaUfccuagcaCfaAfuaaugsusu	8316	AACAUUAUUGUGCUAGGAUUGCU	8584
AD-2123060.1	csasuuauugUfGfCfuaggauugcaL96	8049	VPusdGscadAudCcuagdCaCfaauaaugsusu	8317	AACAUUAUUGUGCUAGGAUUGCU	8585
AD-2123061.1	ususauugUfgCfUfAfggauugcucaL96	8050	VPusGfsagcAfauccuagCfaCfaauaasusg	8318	CAUUAUUGUGCUAGGAUUGCUCU	8586
AD-2123062.1	ususauugugCfUfAfggauugcucaL96	8051	VPusdGsagdCadAuccudAgCfacaauaasusg	8319	CAUUAUUGUGCUAGGAUUGCUCU	8587
AD-2123063.1	ususauugUfgCfUfAfggauugcucaL96	8052	VPusGfsagdCa(Agn)uccuagCfaCfaauaasusg	8320	CAUUAUUGUGCUAGGAUUGCUCU	8588
AD-2123064.1	usasuuguGfcUfAfGfgauugcucuaL96	8053	VPusAfsgagCfaauccuaGfcAfcaauasasu	8321	AUUAUUGUGCUAGGAUUGCUCUC	8589

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123065.1	usasuugugcUfAfGfgauugcucuaL96	8054	VPusdAsgadGcdAauccdTaGfcacaauasasu	8322	AUUAUUGUGCUAGGAUUGCUCUC	8590
AD-2123066.1	asusugugCfuAfGfGfauugcucucaL96	8055	VPusGfsagaGfcaauccuAfgCfacaausasa	8323	UUAUUGUGCUAGGAUUGCUCUCU	8591
AD-2123067.1	asusugugcuAfGfGfauugcucucaL96	8056	VPusdGsagdAgdCaaucdCuAfgcacaausasa	8324	UUAUUGUGCUAGGAUUGCUCUCU	8592
AD-2123068.1	asusugugCfuAfGfGfauuucucucaL96	8057	VPusGfsagdAgdAaauccuAfgCfacaausasa	8325	UUAUUGUGCUAGGAUUGCUCUCU	8593
AD-2123069.1	usgsugcuAfgGfAfUfugcucucuaaL96	8058	VPusUfsagaGfagcaaucCfuAfgcacasasu	8326	AUUGUGCUAGGAUUGCUCUCUAG	8594
AD-2123070.1	usgsugcuagGfAfUfugcucucuaaL96	8059	VPusdTsagdAgdAgcaadTcCfuagcacasasu	8327	AUUGUGCUAGGAUUGCUCUCUAG	8595
AD-2123071.1	cscsagaaGfuGfAfCfuuauuaaacaL96	8060	VPusGfsuuuAfauaagucAfcUfucuggscsu	8328	AGCCAGAAGUGACUUAUUAAACU	8596
AD-2123072.1	cscsagaaguGfAfCfuuauuaaacaL96	8061	VPusdGsuudTadAuaagdTcAfcuucuggscsu	8329	AGCCAGAAGUGACUUAUUAAACU	8597
AD-2123073.1	csasgaagUfgAfCfUfuauuaaacuaL96	8062	VPusAfsguuUfaauaaguCfaCfuucugsgsc	8330	GCCAGAAGUGACUUAUUAAACUA	8598
AD-2123074.1	csasgaagugAfCfUfuauuaaacuaL96	8063	VPusdAsgudTudAauaadGuCfacuucugsgsc	8331	GCCAGAAGUGACUUAUUAAACUA	8599
AD-2123075.1	gsgsaaaaGfgAfCfUfcaagaaaaaaL96	8064	VPusUfsuuuUfcuugaguCfcUfuuuccsusu	8332	AAGGAAAAGGACUCAAGAAAAAU	8600
AD-2123076.1	gsgsaaaaggAfCfUfcaagaaaaaaL96	8065	VPusdTsuudTudCuugadGuCfcuuuuccsusu	8333	AAGGAAAAGGACUCAAGAAAAAU	8601
AD-2123077.1	asasaggaCfuCfAfAfgaaaaauaaaL96	8066	VPusUfsuauUfuuucuugAfgUfccuuususc	8334	GAAAAGGACUCAAGAAAAAUAAU	8602
AD-2123078.1	asasaggacuCfAfAfgaaaaauaaaL96	8067	VPusdTsuadTudTuucudTgAfguccuuususc	8335	GAAAAGGACUCAAGAAAAAUAAU	8603
AD-2123079.1	asasaggaCfuCfAfAfgaaaaauaaaL96	8068	VPusUfsuadTu(Tgn)ucuugAfgUfccuuususc	8336	GAAAAGGACUCAAGAAAAAUAAU	8604
AD-2123080.1	cscsauguGfaAfAfAfgaauguauuaL96	8069	VPusAfsauaCfauucuuuUfcAfcauggsusa	8337	UACCAUGUGAAAAGAAUGUAUUU	8605
AD-2123081.1	cscsaugugaAfAfAfgaauguauuaL96	8070	VPusdAsaudAcdAuucudTuUfcacauggsusa	8338	UACCAUGUGAAAAGAAUGUAUUU	8606
AD-2123082.1	csasugugAfaAfAfGfaauguauuuaL96	8071	VPusAfsaauAfcauucuuUfuCfacaugsgsu	8339	ACCAUGUGAAAAGAAUGUAUUUC	8607
AD-2123083.1	csasugugaaAfAfGfaauguauuuaL96	8072	VPusdAsaadTadCauucdTuUfucacaugsgsu	8340	ACCAUGUGAAAAGAAUGUAUUUC	8608
AD-2123084.1	csasccugCfaAfGfUfuacaaaaaaaL96	8073	VPusUfsuuuUfuguaacuUfgCfaggugsasa	8341	UUCACCUGCAAGUUACAAAAAAA	8609
AD-2123085.1	csasccugcaAfGfUfuacaaaaaaaL96	8074	VPusdTsuudTudTguaadCuUfgcaggugsasa	8342	UUCACCUGCAAGUUACAAAAAAA	8610
AD-2123086.1	csasccugCfaAfGfUfuacaaaaaaaL96	8075	VPusUfsuudTu(Tgn)guaacuUfgCfaggugsasa	8343	UUCACCUGCAAGUUACAAAAAAA	8611
AD-2123087.1	ascscugcAfaGfUfUfacaaaaaaaaL96	8076	VPusUfsuuuUfuuguaacUfuGfcaggusgsa	8344	UCACCUGCAAGUUACAAAAAAAU	8612
AD-2123088.1	ascscugcaaGfUfUfacaaaaaaaaL96	8077	VPusdTsuudTudTuguadAcUfugcaggusgsa	8345	UCACCUGCAAGUUACAAAAAAAU	8613

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123089.1	asasaaaaAfuAfGfUfuugugcauuaL96	8078	VPusAfsaugCfacaaacuAfuUfuuuuusgsu	8346	ACAAAAAAAUAGUUUGUGCAUUG	8614
AD-2123090.1	asasaaaaauAfGfUfuugugcauuaL96	8079	VPusdAsaudGcdAcaaadCuAfuuuuuuusgsu	8347	ACAAAAAAAUAGUUUGUGCAUUG	8615
AD-2123091.1	usgscaaaUfaAfGfCfaaagacuugaL96	8080	VPusCfsaagUfcuuugcuUfaUfuugcasasu	8348	AUUGCAAAUAAGCAAAGACUUGG	8616
AD-2123092.1	usgscaaauaAfGfCfaaagacuugaL96	8081	VPusdCsaadGudCuuugdCuUfauuugcasasu	8349	AUUGCAAAUAAGCAAAGACUUGG	8617
AD-2123093.1	csasaauaAfgCfAfAfagacuuggaaL96	8082	VPusUfsccaAfgucuuugCfuUfauuugscsa	8350	UGCAAAUAAGCAAAGACUUGGAU	8618
AD-2123094.1	csasaauaagCfAfAfagacuuggaaL96	8083	VPusdTsccdAadGucudTgCfuuauuugscsa	8351	UGCAAAUAAGCAAAGACUUGGAU	8619
AD-2123095.1	csasaauaAfgCfAfAfagauuuggaaL96	8084	VPusUfsccdAadAucuuugCfuUfauuugscsa	8352	UGCAAAUAAGCAAAGACUUGGAU	8620
AD-2123096.1	asasauaaGfcAfAfAfgacuuggauaL96	8085	VPusAfsuccAfagucuuuGfcUfuauuusgsc	8353	GCAAAUAAGCAAAGACUUGGAUU	8621
AD-2123097.1	asasauaagcAfAfAfgacuuggauaL96	8086	VPusdAsucdCadAgucudTuGfcuuauuusgsc	8354	GCAAAUAAGCAAAGACUUGGAUU	8622
AD-2123098.1	asasauaaGfcAfAfAfgacuuggauaL96	8087	VPusAfsucdCa(Agn)gucuuuGfcUfuauuusgsc	8355	GCAAAUAAGCAAAGACUUGGAUU	8623
AD-2123099.1	asusaagcAfaAfGfAfcuuggauugaL96	8088	VPusCfsaauCfcaagucuUfuGfcuuaususu	8356	AAAUAAGCAAAGACUUGGAUUGA	8624
AD-2123100.1	asusaagcaaAfGfAfcuuggauugaL96	8089	VPusdCsaadTcdCaagudCuUfugcuuaususu	8357	AAAUAAGCAAAGACUUGGAUUGA	8625
AD-2123101.1	asasgcaaAfgAfCfUfuggauugacaL96	8090	VPusGfsucaAfuccaaguCfuUfugcuusasu	8358	AUAAGCAAAGACUUGGAUUGACU	8626
AD-2123102.1	asasgcaaagAfCfUfuggauugacaL96	8091	VPusdGsucdAadTccaadGuCfuuugcuusasu	8359	AUAAGCAAAGACUUGGAUUGACU	8627
AD-2123103.1	asgscaaaGfaCfUfUfggauugacuaL96	8092	VPusAfsgucAfauccaagUfcUfuugcususa	8360	UAAGCAAAGACUUGGAUUGACUU	8628
AD-2123104.1	asgscaaagaCfUfUfggauugacuaL96	8093	VPusdAsgudCadAuccadAgUfcuuugcususa	8361	UAAGCAAAGACUUGGAUUGACUU	8629
AD-2123105.1	gscsaaagAfcUfUfGfgauugacuuaL96	8094	VPusAfsaguCfaauccaaGfuCfuuugcsusu	8362	AAGCAAAGACUUGGAUUGACUUU	8630
AD-2123106.1	gscsaaagacUfUfGfgauugacuuaL96	8095	VPusdAsagdTcdAauccdAaGfucuuugcsusu	8363	AAGCAAAGACUUGGAUUGACUUU	8631
AD-2123107.1	csasaagaCfuUfGfGfauugacuuuaL96	8096	VPusAfsaagUfcaauccaAfgUfcuuugscsu	8364	AGCAAAGACUUGGAUUGACUUUA	8632
AD-2123108.1	csasaagacuUfGfGfauugacuuuaL96	8097	VPusdAsaadGudCaaucdCaAfgucuuugscsu	8365	AGCAAAGACUUGGAUUGACUUUA	8633
AD-2123109.1	asasagacUfuGfGfAfuugacuuuaaL96	8098	VPusUfsaaaGfucaauccAfaGfucuuusgsc	8366	GCAAAGACUUGGAUUGACUUUAC	8634
AD-2123110.1	asasagacuuGfGfAfuugacuuuaaL96	8099	VPusdTsaadAgdTcaaudCcAfagucuuusgsc	8367	GCAAAGACUUGGAUUGACUUUAC	8635
AD-2123111.1	asasagacUfuGfGfAfuugacuuuaaL96	8100	VPusUfsaadAg(Tgn)caauccAfaGfucuuusgsc	8368	GCAAAGACUUGGAUUGACUUUAC	8636
AD-2123112.1	asasgacuUfgGfAfUfugacuuuacaL96	8101	VPusGfsuaaAfgucaaucCfaAfgucuususg	8369	CAAAGACUUGGAUUGACUUUACA	8637

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123113.1	asasgacuugGfAfUfugacuuuacaL96	8102	VPusdGsuadAadGucaadTcCfaagucuususg	8370	CAAAGACUUGGAUUGACUUUACA	8638
AD-2123114.1	asasgacuUfgGfAfUfugauuuuacaL96	8103	VPusGfsuadAadAucaaucCfaAfgucuususg	8371	CAAAGACUUGGAUUGACUUUACA	8639
AD-2123115.1	asgsacuuGfgAfUfUfgacuuuacaaL96	8104	VPusUfsguaAfagucaauCfcAfagucususu	8372	AAAGACUUGGAUUGACUUUACAU	8640
AD-2123116.1	asgsacuuggAfUfUfgacuuuacaaL96	8105	VPusdTsgudAadAgucadAuCfcaagucususu	8373	AAAGACUUGGAUUGACUUUACAU	8641
AD-2123117.1	asgsacuuGfgAfUfUfgacuuuacaaL96	8106	VPusUfsgudAa(Agn)gucaauCfcAfagucususu	8374	AAAGACUUGGAUUGACUUUACAU	8642
AD-2123118.1	gsascuugGfaUfUfGfacuuuacauaL96	8107	VPusAfsuguAfaagucaaUfcCfaagucsusu	8375	AAGACUUGGAUUGACUUUACAUU	8643
AD-2123119.1	gsascuuggaUfUfGfacuuuacauaL96	8108	VPusdAsugdTadAagucdAaUfccaagucsusu	8376	AAGACUUGGAUUGACUUUACAUU	8644
AD-2123120.1	ascsuuggAfuUfGfAfcuuuacauuaL96	8109	VPusAfsaugUfaaagucaAfuCfcaaguscsu	8377	AGACUUGGAUUGACUUUACAUUC	8645
AD-2123121.1	ascsuuggauUfGfAfcuuuacauuaL96	8110	VPusdAsaudGudAaagudCaAfuccaaguscsu	8378	AGACUUGGAUUGACUUUACAUUC	8646
AD-2123122.1	csusuggaUfuGfAfCfuuuacauucaL96	8111	VPusGfsaauGfuaaagucAfaUfccaagsusc	8379	GACUUGGAUUGACUUUACAUUCA	8647
AD-2123123.1	csusuggauuGfAfCfuuuacauucaL96	8112	VPusdGsaadTgdTaaagdTcAfauccaagsusc	8380	GACUUGGAUUGACUUUACAUUCA	8648
AD-2123124.1	csusuggaUfuGfAfCfuuuacauucaL96	8113	VPusGfsaadTg(Tgn)aaagucAfaUfccaagsusc	8381	GACUUGGAUUGACUUUACAUUCA	8649
AD-2123125.1	ususggauUfgAfCfUfuuacauucaaL96	8114	VPusUfsgaaUfguaaaguCfaAfuccaasgsu	8382	ACUUGGAUUGACUUUACAUUCAU	8650
AD-2123126.1	ususggauugAfCfUfuuacauucaaL96	8115	VPusdTsgadAudGuaaadGuCfaauccaasgsu	8383	ACUUGGAUUGACUUUACAUUCAU	8651
AD-2123127.1	ususggauUfgAfCfUfuuauauucaaL96	8116	VPusUfsgadAudAuaaaguCfaAfuccaasgsu	8384	ACUUGGAUUGACUUUACAUUCAU	8652
AD-2123128.1	gsasuugaCfuUfUfAfcauucaucaaL96	8117	VPusUfsgauGfaauguaaAfgUfcaaucscsa	8385	UGGAUUGACUUUACAUUCAUCAU	8653
AD-2123129.1	gsasuugacuUfUfAfcauucaucaaL96	8118	VPusdTsgadTgdAaugudAaAfgucaaucscsa	8386	UGGAUUGACUUUACAUUCAUCAU	8654
AD-2123130.1	gsasuugaCfuUfUfAfcauucaucaaL96	8119	VPusUfsgadTg(Agn)auguaaAfgUfcaaucscsa	8387	UGGAUUGACUUUACAUUCAUCAU	8655
AD-2123131.1	asusugacUfuUfAfCfauucaucauaL96	8120	VPusAfsugaUfgaauguaAfaGfucaauscsc	8388	GGAUUGACUUUACAUUCAUCAUU	8656
AD-2123132.1	asusugacuuUfAfCfauucaucauaL96	8121	VPusdAsugdAudGaaugdTaAfagucaauscsc	8389	GGAUUGACUUUACAUUCAUCAUU	8657
AD-2123133.1	asusugacUfuUfAfCfauuuaucauaL96	8122	VPusAfsugdAudAaauguaAfaGfucaauscsc	8390	GGAUUGACUUUACAUUCAUCAUU	8658
AD-2123134.1	ususgacuUfuAfCfAfuucaucauuaL96	8123	VPusAfsaugAfugaauguAfaAfgucaasusc	8391	GAUUGACUUUACAUUCAUCAUUU	8659
AD-2123135.1	ususgacuuuAfCfAffuucaucauuaL96	8124	VPusdAsaudGadTgaaudGuAfaagucaasusc	8392	GAUUGACUUUACAUUCAUCAUUU	8660
AD-2123136.1	ususgacuUfuAfCfAfuucaucauuaL96	8125	VPusAfsaudGa(Tgn)gaauguAfaAfgucaasusc	8393	GAUUGACUUUACAUUCAUCAUUU	8661

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123137.1	csasuaucCfuGfAfAfauucaugguaL96	8126	VPusAfsccaUfgaauuucAfgGfauaugsusg	8394	CACAUAUCCUGAAAUUCAUGGUU	8662
AD-2123138.1	csasuauccuGfAfAfauucaugguaL96	8127	VPusdAsccdAudGaauudTcAfggauaugsusg	8395	CACAUAUCCUGAAAUUCAUGGUU	8663
AD-2123139.1	asusauccUfgAfAfAfuucaugguuaL96	8128	VPusAfsaccAfugaauuuCfaGfgauausgsu	8396	ACAUAUCCUGAAAUUCAUGGUUU	8664
AD-2123140.1	asusauccugAfAfAfuucaugguuaL96	8129	VPusdAsacdCadTgaaudTuCfaggauausgsu	8397	ACAUAUCCUGAAAUUCAUGGUUU	8665
AD-2123141.1	usasuccuGfaAfAfUfucaugguuuaL96	8130	VPusAfsaacCfaugaauuUfcAfggauasusg	8398	CAUAUCCUGAAAUUCAUGGUUUC	8666
AD-2123142.1	usasuccugaAfAfUfucaugguuuaL96	8131	VPusdAsaadCcdAugaadTuUfcaggauasusg	8399	CAUAUCCUGAAAUUCAUGGUUUC	8667
AD-2123143.1	usasuccuGfaAfAfUfucaugguuuaL96	8132	VPusAfsaadCc(Agn)ugaauuUfcAfggauasusg	8400	CAUAUCCUGAAAUUCAUGGUUUC	8668
AD-2123144.1	asasuacaGfcUfGfGfuggaguucuaL96	8133	VPusAfsgaaCfuccaccaGfcUfguauusasg	8401	CUAAUACAGCUGGUGGAGUUCUA	8669
AD-2123145.1	asasuacagcUfGfGfuggaguucuaL96	8134	VPusdAsgadAcdTccacdCaGfcuguauusasg	8402	CUAAUACAGCUGGUGGAGUUCUA	8670
AD-2123146.1	asasuacaGfcUfGfGfuggaguucuaL96	8135	VPusAfsgadAc(Tgn)ccaccaGfcUfguauusasg	8403	CUAAUACAGCUGGUGGAGUUCUA	8671
AD-2123147.1	ascsagcuGfgUfGfGfaguucuaucaL96	8136	VPusGfsauaGfaacuccaCfcAfgcugusasu	8404	AUACAGCUGGUGGAGUUCUAUCA	8672
AD-2123148.1	ascsagcuggUfGfGfaguucuaucaL96	8137	VPusdGsaudAgdAacucdCaCfcagcugusasu	8405	AUACAGCUGGUGGAGUUCUAUCA	8673
AD-2123149.1	ascsagcuGfgUfGfGfaguucuaucaL96	8138	VPusGfsaudAg(Agn)acuccaCfcAfgcugusasu	8406	AUACAGCUGGUGGAGUUCUAUCA	8674
AD-2123150.1	asasggaaAfaGfGfAfcucaagaaaaL96	8139	VPusUfsuucUfugaguccUfuUfuccuuscsa	8407	UGAAGGAAAAGGACUCAAGAAAA	8675
AD-2123151.1	asasggaaaaGfGfAfcucaagaaaaL96	8140	VPusdTsuudCudTgagudCcUfuuuccuuscsa	8408	UGAAGGAAAAGGACUCAAGAAAA	8676
AD-2123152.1	asasggaaAfaGfGfAfcucaagaaaaL96	8141	VPusUfsuudCu(Tgn)gaguccUfuUfuccuuscsa	8409	UGAAGGAAAAGGACUCAAGAAAA	8677
AD-2123153.1	asusuucaCfcUfGfCfaaguuacaaaL96	8142	VPusUfsuguAfacuugcaGfgUfgaaausasc	8410	GUAUUUCACCUGCAAGUUACAAA	8678
AD-2123154.1	asusuucaccUfGfCfaaguuacaaaL96	8143	VPusdTsugdTadAcuugdCaGfgugaaausasc	8411	GUAUUUCACCUGCAAGUUACAAA	8679
AD-2123155.1	asusuucaCfcUfGfCfaaguuacaaaL96	8144	VPusUfsugdTa(Agn)cuugcaGfgUfgaaausasc	8412	GUAUUUCACCUGCAAGUUACAAA	8680
AD-2123156.1	ususaugcCfaAfAfUfaugaguucuaL96	8145	VPusAfsgaaCfucauauuUfgGfcauaasusu	8413	AAUUAUGCCAAAUAUGAGUUCUU	8681
AD-2123157.1	ususaugccaAfAfUffaugaguucuaL96	8146	VPusdAsgadAcdTcauadTuUfggcauaasusu	8414	AAUUAUGCCAAAUAUGAGUUCUU	8682
AD-2123158.1	csasaauaUfgAfGfUfucuuuaaaaaL96	8147	VPusUfsuuuAfaagaacuCfaUfauuugsgsc	8415	GCCAAAUAUGAGUUCUUUAAAAA	8683
AD-2123159.1	csasaauaugAfGfUfucuuuaaaaaL96	8148	VPusdTsuudTadAagaadCuCfauauuugsgsc	8416	GCCAAAUAUGAGUUCUUUAAAAA	8684
AD-2123160.1	cscsagagCfaUfAfUfgguaucuuuaL96	8149	VPusAfsaagAfuaccauaUfgCfucuggsasa	8417	UUCCAGAGCAUAUGGUAUCUUUU	8685

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123161.1	cscsagagcaUfAfUfgguaucuuuaL96	8150	VPusdAsaadGadTaccadTaUfgcucuggsasa	8418	UUCCAGAGCAUAUGGUAUCUUUU	8686
AD-2123162.1	asgsagcaUfaUfGfGfuaucuuuugaL96	8151	VPusCfsaaaAfgauaccaUfaUfgcucusgsg	8419	CCAGAGCAUAUGGUAUCUUUUGC	8687
AD-2123163.1	asgsagcauaUfGfGfuaucuuuugaL96	8152	VPusdCsaadAadGauacdCaUfaugcucusgsg	8420	CCAGAGCAUAUGGUAUCUUUUGC	8688
AD-2123164.1	gsasgcauAfuGfGfUfaucuuuugcaL96	8153	VPusGfscaaAfagauaccAfuAfugcucsusg	8421	CAGAGCAUAUGGUAUCUUUUGCA	8689
AD-2123165.1	gsasgcauauGfGfUfaucuuuugcaL96	8154	VPusdGscadAadAgauadCcAfuaugcucsusg	8422	CAGAGCAUAUGGUAUCUUUUGCA	8690
AD-2123166.1	asgscauaUfgGfUfAfucuuuugcaaL96	8155	VPusUfsgcaAfaagauacCfaUfaugcuscsu	8423	AGAGCAUAUGGUAUCUUUUGCAA	8691
AD-2123167.1	asgscauaugGfUfAfucuuuugcaaL96	8156	VPusdTsgcdAadAagaudAcCfauaugcuscsu	8424	AGAGCAUAUGGUAUCUUUUGCAA	8692
AD-2123168.1	asgsauguUfuCfUfGfaguucaagcaL96	8157	VPusGfscuuGfaacucagAfaAfcaucusgsc	8425	GCAGAUGUUUCUGAGUUCAAGCA	8693
AD-2123169.1	asgsauguuuCfUfGfaguucaagcaL96	8158	VPusdGscudTgdAacucdAgAfaacaucusgsc	8426	GCAGAUGUUUCUGAGUUCAAGCA	8694
AD-2123170.1	asgsauguUfuCfUfGfaguucaagcaL96	8159	VPusGfscudTg(Agn)acucagAfaAfcaucusgsc	8427	GCAGAUGUUUCUGAGUUCAAGCA	8695
AD-2123171.1	asusguuuCfuGfAfGfuucaagcacaL96	8160	VPusGfsugcUfugaacucAfgAfaacauscsu	8428	AGAUGUUUCUGAGUUCAAGCACA	8696
AD-2123172.1	asusguuucuGfAfGfuucaagcacaL96	8161	VPusdGsugdCudTgaacdTcAfgaaacauscsu	8429	AGAUGUUUCUGAGUUCAAGCACA	8697
AD-2123173.1	asusguuuCfuGfAfGfuucaagcacaL96	8162	VPusGfsugdCu(Tgn)gaacucAfgAfaacauscsu	8430	AGAUGUUUCUGAGUUCAAGCACA	8698
AD-2123174.1	gsusuucuGfaGfUfUfcaagcacauaL96	8163	VPusAfsuguGfcuugaacUfcAfgaaacsasu	8431	AUGUUUCUGAGUUCAAGCACAUA	8699
AD-2123175.1	gsusuucugaGfUfUfcaagcacauaL96	8164	VPusdAsugdTgdCuugadAcUfcagaaacsasu	8432	AUGUUUCUGAGUUCAAGCACAUA	8700
AD-2123176.1	gsusuucuGfaGfUfUfcaaucacauaL96	8165	VPusAfsugdTgdAuugaacUfcAfgaaacsasu	8433	AUGUUUCUGAGUUCAAGCACAUA	8701
AD-2123177.1	asusccugAfaAfUfUfcaugguuucaL96	8166	VPusGfsaaaCfcaugaauUfuCfaggausasu	8434	AUAUCCUGAAAUUCAUGGUUUCU	8702
AD-2123178.1	asusccugaaAfUfUfcaugguuucaL96	8167	VPusdGsaadAcdCaugadAuUfucaggausasu	8435	AUAUCCUGAAAUUCAUGGUUUCU	8703
AD-2123179.1	asusccugAfaAfUfUfcauuguuucaL96	8168	VPusGfsaadAcdAaugaauUfuCfaggausasu	8436	AUAUCCUGAAAUUCAUGGUUUCU	8704
AD-2123180.1	gsasaauuCfaUfGfGfuuucuuacaaL96	8169	VPusUfsguaAfgaaaccaUfgAfauuucsasg	8437	CUGAAAUUCAUGGUUUCUUACAU	8705
AD-2123181.1	gsasaauucaUfGfGfuuucuuacaaL96	8170	VPusdTsgudAadGaaacdCaUfgaauuucsasg	8438	CUGAAAUUCAUGGUUUCUUACAU	8706
AD-2123182.1	gsasaauuCfaUfGfGfuuuuuuacaaL96	8171	VPusUfsgudAadAaaaccaUfgAfauuucsasg	8439	CUGAAAUUCAUGGUUUCUUACAU	8707
AD-2123183.1	ususcaugGfuUfUfCfuuacaugcgaL96	8172	VPusCfsgcaUfguaagaaAfcCfaugaasusu	8440	AAUUCAUGGUUUCUUACAUGCGA	8708
AD-2123184.1	ususcaugguUfUfCfuuacaugcgaL96	8173	VPusdCsgcdAudGuaagdAaAfccaugaasusu	8441	AAUUCAUGGUUUCUUACAUGCGA	8709

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123185.1	ususcaugGfuUfUfCfuuauaugcgaL96	8174	VPusCfsgcdAudAuaagaaAfcCfaugaasusu	8442	AAUUCAUGGUUUCUUACAUGCGA	8710
AD-2123186.1	uscsauggUfuUfCfUfuacaugcgaaL96	8175	VPusUfscgcAfuguaagaAfaCfcaugasasu	8443	AUUCAUGGUUUCUUACAUGCGAA	8711
AD-2123187.1	uscsaugguuUfCfUfuacaugcgaaL96	8176	VPusdTscgdCadTguaadGaAfaccaugasasu	8444	AUUCAUGGUUUCUUACAUGCGAA	8712
AD-2123188.1	uscsauggUfuUfCfUfuacaugcgaaL96	8177	VPusUfscgdCa(Tgn)guaagaAfaCfcaugasasu	8445	AUUCAUGGUUUCUUACAUGCGAA	8713
AD-2123189.1	asgsggaaAfgAfAfGfucuuggaaaaL96	8178	VPusUfsuucCfaagacuuCfuUfucccusgsu	8446	ACAGGGAAAGAAGUCUUGGAAAA	8714
AD-2123190.1	asgsggaaagAfAfGfucuuggaaaaL96	8179	VPusdTsuudCcdAagacdTuCfuuucccusgsu	8447	ACAGGGAAAGAAGUCUUGGAAAA	8715
AD-2123191.1	asgsggaaAfgAfAfGfucuuggaaaaL96	8180	VPusUfsuudCc(Agn)agacuuCfuUfucccusgsu	8448	ACAGGGAAAGAAGUCUUGGAAAA	8716
AD-2123192.1	gsgsaaagAfaGfUfCfuuggaaaaaaL96	8181	VPusUfsuuuUfccaagacUfuCfuuuccscsu	8449	AGGGAAAGAAGUCUUGGAAAAAA	8717
AD-2123193.1	gsgsaaagaaGfUfCfuuggaaaaaaL96	8182	VPusdTsuudTudCcaagdAcUfucuuuccscsu	8450	AGGGAAAGAAGUCUUGGAAAAAA	8718
AD-2123194.1	gsgsaaagAfaGfUfCfuuguaaaaaaL96	8183	VPusUfsuudTudAcaagacUfuCfuuuccscsu	8451	AGGGAAAGAAGUCUUGGAAAAAA	8719
AD-2123195.1	gsasaagaAfgUfCfUfuggaaaaaaaL96	8184	VPusUfsuuuUfuccaagaCfuUfcuuucscsc	8452	GGGAAAGAAGUCUUGGAAAAAAA	8720
AD-2123196.1	gsasaagaagUfCfUfuggaaaaaaL96	8185	VPusdTsuudTudTccaadGaCfuucuuucscsc	8453	GGGAAAGAAGUCUUGGAAAAAAA	8721
AD-2123197.1	gsasaagaAfgUfCfUfuggaaaaaaaL96	8186	VPusUfsuudTu(Tgn)ccaagaCfuUfcuuucscsc	8454	GGGAAAGAAGUCUUGGAAAAAAA	8722
AD-2123198.1	asasagaaGfuCfUfUfgggaaaaaaaL96	8187	VPusUfsuuuUfuuccaagAfcUfucuuuscsc	8455	GGAAAGAAGUCUUGGAAAAAAAU	8723
AD-2123199.1	asasagaaguCfUfUfggaaaaaaaL96	8188	VPusdTsuudTudTuccadAgAfcuucuuuscsc	8456	GGAAAGAAGUCUUGGAAAAAAAU	8724
AD-2123200.1	asasgucuUfgGfAfAfaaaaauuuaaL96	8189	VPusUfsaaaUfuuuuuucCfaAfgacuuscsu	8457	AGAAGUCUUGGAAAAAAAUUUAC	8725
AD-2123201.1	asasgucuugGfAfAfaaaaauuuaaL96	8190	VPusdTsaadAudTuuudTcCfaagacuuscsu	8458	AGAAGUCUUGGAAAAAAAUUUAC	8726
AD-2123202.1	asgsucuuGfgAfAfAfaaaauuuacaL96	8191	VPusGfsuaaAfuuuuuuuCfcAfagacususc	8459	GAAGUCUUGGAAAAAAAUUUACU	8727
AD-2123203.1	asgsucuuggAfAfAfaaaauuuacaL96	8192	VPusdGsuadAadTuuudTuCfcaagacususc	8460	GAAGUCUUGGAAAAAAAUUUACU	8728
AD-2123204.1	asasccgcGfgCfAfUfuugcaguuuaL96	8193	VPusAfsaacUfgcaaaugCfcGfcgguuscsc	8461	GGAACCGCGGCAUUUGCAGUUUU	8729
AD-2123205.1	asasccgcggCfAfUfUfuugcaguuuaL96	8194	VPusdAsaadCudGcaaadTgCfcgcgguuscsc	8462	GGAACCGCGGCAUUUGCAGUUUU	8730
AD-2123206.1	asasccgcGfgCfAfUfuuguaguuuaL96	8195	VPusAfsaadCudAcaaaugCfcGfcgguuscsc	8463	GGAACCGCGGCAUUUGCAGUUUU	8731
AD-2123207.1	gscsauuuGfcAfGfUfuuuucagcgaL96	8196	VPusCfsgcuGfaaaaacuGfcAfaaugcscsg	8464	CGGCAUUUGCAGUUUUUCAGCGA	8732
AD-2123208.1	gscsauuugcAfGfUfuuuucagcgaL96	8197	VPusdCsgcdTgdAaaaadCuGfcaaaugcscsg	8465	CGGCAUUUGCAGUUUUUCAGCGA	8733

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123209.1	gscsauuuGfcAfGf Ufuuuucagcga L96	8198	VPusCfsgcdTg(Agn)a aaacuGfcAfaaugcscsg	8466	CGGCAUUUGCAG UUUUUCAGCGA	8734
AD-2123210.1	asusuugcAfgUfUf Ufuucagcgaaa L96	8199	VPusUfsucgCfugaaaa aCfuGfcaaausgsc	8467	GCAUUUGCAGUU UUUCAGCGAAU	8735
AD-2123211.1	asusuugcagUfUfU fuucagcgaaa L96	8200	VPusdTsucdGcdTgaaa dAaCfugcaaausgsc	8468	GCAUUUGCAGUU UUUCAGCGAAU	8736
AD-2123212.1	asusuugcAfgUfUf Ufuucagcgaaa L96	8201	VPusUfsucdGc(Tgn)g aaaaaCfuGfcaaausgsc	8469	GCAUUUGCAGUU UUUCAGCGAAU	8737
AD-2123213.1	ususgcagUfuUfUf Ufcagcgaauua L96	8202	VPusAfsauuCfgcugaa aAfaCfugcaasasu	8470	AUUUGCAGUUUU UCAGCGAAUUU	8738
AD-2123214.1	ususgcaguuUfUfU fcagcgaauua L96	8203	VPusdAsaudTcdGcug adAaAfacugcaasasu	8471	AUUUGCAGUUUU UCAGCGAAUUU	8739
AD-2123215.1	ususgcagUfuUfUf Ufcagugaauua L96	8204	VPusAfsaudTcdAcuga aaAfaCfugcaasasu	8472	AUUUGCAGUUUU UCAGCGAAUUU	8740
AD-2123216.1	ususucagCfgAfAf Ufuuggcaauaa L96	8205	VPusUfsauuGfccaaau uCfgCfugaaasasa	8473	UUUUUCAGCGAA UUUGGCAAUAG	8741
AD-2123217.1	ususucagcgAfAfU fuuggcaauaa L96	8206	VPusdTsaudTgdCcaaa dTuCfgcugaaasasa	8474	UUUUUCAGCGAA UUUGGCAAUAG	8742
AD-2123218.1	ususucagCfgAfAf Ufuugucaauaa L96	8207	VPusUfsaudTgdAcaaa uuCfgCfugaaasasa	8475	UUUUUCAGCGAA UUUGGCAAUAG	8743
AD-2123219.1	gsasauuuGfgCfAf Afuagugauaua L96	8208	VPusAfsuauCfacuauu gCfcAfaauucsgsc	8476	GCGAAUUUGGCA AUAGUGAUAUU	8744
AD-2123220.1	gsasauuuggCfAfA fuagugauaua L96	8209	VPusdAsuadTcdAcua udTgCfcaaauucsgsc	8477	GCGAAUUUGGCA AUAGUGAUAUU	8745
AD-2123221.1	usgsgcaaUfaGfUf Gfauauuuauga L96	8210	VPusCfsauaAfauaucac UfaUfugccasasa	8478	UUUGGCAAUAGU GAUAUUUAUGU	8746
AD-2123222.1	usgsgcaauaGfUfG fauauuuauga L96	8211	VPusdCsaudAadAuau cdAcUfauugccasasa	8479	UUUGGCAAUAGU GAUAUUUAUGU	8747
AD-2123223.1	gsgscaauAfgUfGf AfuauuuauguaL96	8212	VPusAfscauAfaauauc aCfuAfuugccsasa	8480	UUGGCAAUAGUG AUAUUUAUGUG	8748
AD-2123224.1	gsgscaauagUfGfA fuauuuauguaL96	8213	VPusdAscadTadAaua udCaCfuauugccsasa	8481	UUGGCAAUAGUG AUAUUUAUGUG	8749
AD-2123225.1	gscsaauaGfuGfAf Ufauuuauguga L96	8214	VPusCfsacaUfaaauauc AfcUfauugcscsa	8482	UGGCAAUAGUGA UAUUUAUGUGU	8750
AD-2123226.1	gscsaauaguGfAfU fauuuaugugaL96	8215	VPusdCsacdAudAaau adTcAfcuauugcscsa	8483	UGGCAAUAGUGA UAUUUAUGUGU	8751
AD-2123227.1	ascsauggAfgCfAf Cfcgacuaacua L96	8216	VPusAfsguuAfgucggu gCfuCfcaugususu	8484	AAACAUGGAGCA CCGACUAACUA	8752
AD-2123228.1	ascsauggagCfAfCf cgacuaacua L96	8217	VPusdAsgudTadGucg gdTgCfuccaugususu	8485	AAACAUGGAGCA CCGACUAACUA	8753
AD-2123229.1	ascsauggAfgCfAf Cfcgauuaacua L96	8218	VPusAfsgudTadAucg gugCfuCfcaugususu	8486	AAACAUGGAGCA CCGACUAACUA	8754
AD-2123230.1	csusaacuAfuGfGf Afuucugcuuua L96	8219	VPusAfsaagCfagaaucc AfuAfguuagsusc	8487	GACUAACUAUGG AUUCUGCUUUA	8755
AD-2123231.1	csusaacuauGfGfA fuucugcuuua L96	8220	VPusdAsaadGcdAgaa udCcAfuaguuagsusc	8488	GACUAACUAUGG AUUCUGCUUUA	8756
AD-2123232.1	csusaacuAfuGfGf Afuucugcuuua L96	8221	VPusAfsaadGc(Agn)g aauccAfuAfguuagsusc	8489	GACUAACUAUGG AUUCUGCUUUA	8757

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-2123233.1	usgscagcUfgUfAfCfcagaauuauaL96	8222	VPusAfsuaaUfucugguaCfaGfcugcasusg	8490	CAUGCAGCUGUACCAGAAUUAUA	8758
AD-2123234.1	usgscagcugUfAfCfcagaauuauaL96	8223	VPusdAsuadAudTcuggdTaCfagcugcasusg	8491	CAUGCAGCUGUACCAGAAUUAUA	8759
AD-2123235.1	gscsuguaCfcAfGfAfauuauaugcaL96	8224	VPusGfscauAfuaauucuGfgUfacagcsusg	8492	CAGCUGUACCAGAAUUAUAUGCA	8760
AD-2123236.1	gscsuguaccAfGfAfauuauaugcaL96	8225	VPusdGscadTadTaauudCuGfguacagcsusg	8493	CAGCUGUACCAGAAUUAUAUGCA	8761
AD-2123237.1	csusguacCfaGfAfAfuuauaugcaaL96	8226	VPusUfsgcaUfauaauucUfgGfuacagscsu	8494	AGCUGUACCAGAAUUAUAUGCAU	8762
AD-2123238.1	csusguaccaGfAfAfuuauaugcaaL96	8227	VPusdTsgcdAudAuaaudTcUfgguacagscsu	8495	AGCUGUACCAGAAUUAUAUGCAU	8763
AD-2123239.1	csusguacCfaGfAfAfuuauaugcaaL96	8228	VPusUfsgcdAu(Agn)uaauucUfgGfuacagscsu	8496	AGCUGUACCAGAAUUAUAUGCAU	8764
AD-2123240.1	usgsuaccAfgAfAfUfuauaugcauaL96	8229	VPusAfsugcAfuauaauuCfuGfguacasgsc	8497	GCUGUACCAGAAUUAUAUGCAUC	8765
AD-2123241.1	usgsuaccagAfAfUfuauaugcauaL96	8230	VPusdAsugdCadTauaadTuCfugguacasgsc	8498	GCUGUACCAGAAUUAUAUGCAUC	8766
AD-2123242.1	ascscagaAfuUfAfUfaugcauccaaL96	8231	VPusUfsggaUfgcauauaAfuUfcuggusasc	8499	GUACCAGAAUUAUAUGCAUCCAU	8767
AD-2123243.1	ascscagaauUfAfUfaugcauccaaL96	8232	VPusdTsggdAudGcauadTaAfuucuggusasc	8500	GUACCAGAAUUAUAUGCAUCCAU	8768
AD-2123244.1	ascscagaAfuUfAfUfauguauccaaL96	8233	VPusUfsggdAudAcauauaAfuUfcuggusasc	8501	GUACCAGAAUUAUAUGCAUCCAU	8769

Table 6. Human GRB14 Unmodified Sense and Antisense Sequences Designed Without VP Modification

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Range	Antisense Sequence 5' to 3'	SEQ ID NO	Range
AD-2217245.1	CAAAACUUUCGUACUGUCAAA	8770	1589-1609	UUUGACAGUACGAAAGUUUUGGG	8784	1587-1609
AD-2217246.1	AAGACUUGGAUUGACUUUACA	8771	1949-1969	UGUAAAGUCAAUCCAAGUCUUUG	8785	1947-1969
AD-2217247.1	AAGACUUGGAUUGACUUUACA	8772	1949-1969	UGUAAAGUCAATCCAAGUCUUUG	8786	1947-1969
AD-2217248.1	UUGGAUUGACUUUACAUUCAA	8773	1954-1974	UUGAAUGUAAAGUCAAUCCAAGU	8787	1952-1974
AD-2217249.1	AUUGACUUUACAUUCAUCAUA	8774	1958-1978	UAUGAUGAAUGUAAAGUCAAUCC	8788	1956-1978
AD-2217250.1	AUUGACUUUACAUUCAUCAUA	8775	1958-1978	UAUGAUGAAUGTAAAGUCAAUCC	8789	1956-1978
AD-2217251.1	UUGACUUUACAUUCAUCAUUA	8776	1959-1979	UAAUGAUGAAUGUAAAGUCAAUC	8790	1957-1979
AD-2217252.1	UUGACUUUACAUUCAUCAUUA	8777	1959-1979	UAAUGATGAAUGUAAAGUCAAUC	8791	1957-1979

AD-2217253.1	UUGACUUUACA UUCAUCAUUA	8778	1959-1979	UAAUGATGAAUG UAAAGUCAAUC	8792	1957-1979
AD-2217254.1	UAUCCUGAAAU UCAUGGUUUA	8779	873-893	UAAACCAUGAAT UUCAGGAUAUG	8793	871-893
AD-2217255.1	UAUCCUGAAAU UCAUGGUUUA	8780	873-893	UAAACCAUGAAU UUCAGGAUAUG	8794	871-893
AD-2217257.1	UUAUGCCAAAU AUGAGUUCUA	8781	743-763	UAGAACTCAUAT UUGGCAUAAUU	8795	741-763
AD-2217258.1	AGAGCAUAUGG UAUCUUUUGA	8782	788-808	UCAAAAGAUACC AUAUGCUCUGG	8796	786-808
AD-2217262.1	UGCAAGUUGAA ACAUUAUUGA	8783	1758-1778	UCAATAAUGUUT CAACUUGCAAG	8797	1756-1778

Table 7. Human GRB14 Modified Sense and Antisense Sequences Designed Without VP Modification

Duplex ID	Sense Sequence 5' to 3'	SEQ ID NO	Antisense Sequence 5' to 3'	SEQ ID NO	mRNA Target Sequence	SEQ ID NO
AD-2217245.1	csasaaacUfuUfCfGfuacugucaaaL96	8798	usUfsugaCfaguacgaAfaGfuuuugsgsg	8812	CCCAAAACUUUCGUACUGUCAAU	8826
AD-2217246.1	asasgacuUfgGfAfUfugacuuuacaL96	8799	usGfsuaaAfgucaaucCfaAfgucuususg	8813	CAAAGACUUGGAUUGACUUUACA	8827
AD-2217247.1	asasgacuugGfAfUfugacuuuacaL96	8800	usdGsuadAadGucaadTcCfaagucuususg	8814	CAAAGACUUGGAUUGACUUUACA	8828
AD-2217248.1	ususggauUfgAfCfUfuuacauucaaL96	8801	usUfsgaaUfguaaaguCfaAfuccaasgsu	8815	ACUUGGAUUGACUUUACAUUCAU	8829
AD-2217249.1	asusugacUfuUfAfCfauucaucauaL96	8802	usAfsugaUfgaauguaAfaGfucaauscsc	8816	GGAUUGACUUUACAUUCAUCAUU	8830
AD-2217250.1	asusugacuuUfAfCfauucaucauaL96	8803	usdAsugdAudGaaugdTaAfagucaauscsc	8817	GGAUUGACUUUACAUUCAUCAUU	8831
AD-2217251.1	ususgacuUfuAfCfAfuucaucauuaL96	8804	usAfsaugAfugaauguAfaAfgucaasusc	8818	GAUUGACUUUACAUUCAUCAUUU	8832
AD-2217252.1	ususgacuuuAfCfAfuucaucauuaL96	8805	usdAsaudGadTgaaudGuAfaagucaasusc	8819	GAUUGACUUUACAUUCAUCAUUU	8833
AD-2217253.1	ususgacuUfuAfCfAfuucaucauuaL96	8806	usAfsaudGa(Tgn)gaauguAfaAfgucaasusc	8820	GAUUGACUUUACAUUCAUCAUUU	8834
AD-2217254.1	usasuccugaAfAfUfucaugguuuaL96	8807	usdAsaadCcdAugaadTuUfcaggauasusg	8821	CAUAUCCUGAAAUUCAUGGUUUC	8835
AD-2217255.1	usasuccuGfaAfAfUfucaugguuuaL96	8808	usAfsaadCc(Agn)ugaauuUfcAfggauasusg	8822	CAUAUCCUGAAAUUCAUGGUUUC	8836
AD-2217257.1	ususaugccaAfAfUfaugaguucuaL96	8809	usdAsgadAcdTcauadTuUfggcauaasusu	8823	AAUUAUGCCAAAUAUGAGUUCUU	8837
AD-2217258.1	asgsagcaUfaUfGfGfuaucuuuugaL96	8810	usCfsaaaAfgauaccaUfaUfgcucusgsg	8824	CCAGAGCAUAUGGUAUCUUUUGC	8838
AD-2217262.1	usgscaaguuGfAfAfacauuauugaL96	8811	usdCsaadTadAuguudTcAfacuugcasasg	8825	CUUGCAAGUUGAAACAUUAUUGU	8839

Example 2. *In vitro* screening methods

This Example describes *in vitro* Hep3B, Primary Human Hepatocytes, and Primary Cynomolgus Hepatocytes screening.

Cell culture and transfections:

Hep3B cells (ATCC, Manassas, VA) were grown to near confluence at 37°C in an atmosphere of 5% CO2 in Eagle's Minimum Essential Medium (Gibco) supplemented with 10% FBS (ATCC) before being released from the plate by trypsinization. Transfection was carried out by adding 14.7 µl of Opti-MEM plus 0.3 µl of Lipofectamine RNAiMax per well (Invitrogen, Carlsbad CA. cat # 13778-150) to 5 µl of each siRNA duplex to an individual well in a 96-well plate with 4 replicates of each siRNA duplex. The mixture was then incubated at room temperature for 15 minutes. Eighty µl of complete growth media without antibiotic containing ~1.5 x10^4 Hep3B cells were then added to the siRNA mixture. Cells were incubated for 24 hours prior to RNA purification. Multi-dose experiments were performed at 10 nM, 1 nM, and 0.1 nM final duplex concentration.

Primary Human Hepatocytes (BioIVT) were transfected by adding 4.9µl of Opti-MEM plus 0.1µl of RNAiMAX per well (Invitrogen, Carlsbad CA. cat # 13778-150) to 5µl of siRNA duplexes per well, with 4 replicates of each siRNA duplex, into a 384-well plate, and incubated at room temperature for 15 minutes. Thirty-five µl of InVitroGRO CP plating media (BioIVT) containing ~15 x10^3 cells were then added to the siRNA mixture. Cells were incubated for 48 hours prior to RNA purification. Multi-dose experiments were performed at 250nM, 100nM, 10 nM, and 1 nM.

Primary Cynomolgus Hepatocytes (BioIVT) were transfected by adding 4.9µl of Opti-MEM plus 0.1µl of RNAiMAX per well (Invitrogen, Carlsbad CA. cat # 13778-150) to 5µl of siRNA duplexes per well, with 4 replicates of each siRNA duplex, into a 384-well plate, and incubated at room temperature for 15 minutes. Thirty-five µl of InVitroGRO CP plating media (BioIVT) containing ~5 x10^3 cells were then added to the siRNA mixture. Cells were incubated for 48 hours prior to RNA purification. Multi-dose experiments were performed at 250nM, 100nM, 10 nM, and 1 nM.

Free uptake:

Free uptake assays were performed to assess the pharmacodynamic properties of the siRNAs. Free uptake assay was performed similarly to the transfection assay without using Lipofectamine RNAimax and cells were incubated for 48 hours prior to the RNA purification. Experiments were performed essentially as described in Agarwal S., *Nucleic Acid. Ther.* (2021) 31(4):309-315. Dose response experiments were performed at various final duplex concentrations.

LogIC50 assay:

The IC50 experiments were then performed to characterize the potency of each siRNA duplex by determining the concentration at which 50% of the mRNA was remaining. Free uptake assays or transfection assays of PHH or PCH cells were performed as described above, except various log concentrations of selected siRNA duplexes were used in the assays. The percent of message remaining was determined and the LogIC50 was calculated.

Total RNA isolation using DYNABEADS mRNA Isolation Kit:

RNA is isolated using an automated protocol on a BioTek-EL406 platform using DYNABEADs (Invitrogen, cat#61012). Briefly, 70ul of Lysis/Binding Buffer and 10ul of lysis buffer containing 3µl of magnetic beads are added to the plate with cells. Plates were incubated on an electromagnetic shaker for 10 minutes at room temperature and then magnetic beads are captured and the supernatant is removed. Bead-bound RNA is then washed 2 times with 150ul Wash Buffer A and once with Wash Buffer B. Beads are then washed with 150µl Elution Buffer, re-captured and supernatant removed.

cDNA synthesis using ABI High capacity cDNA reverse transcription kit (Applied Biosystems, Foster City, CA, Cat #4368813):

Ten µl of a master mix containing 1µl 10X Buffer, 0.4µl 25X dNTPs, 1µl 10x Random primers, 0.5µl Reverse Transcriptase, 0.5µl RNase inhibitor and 6.6µl of H_2O per reaction are added to RNA isolated above. Plates are sealed, mixed, and incubated on an electromagnetic shaker for 10 minutes at room temperature, followed by 2h at 37°C.

Real time PCR:

Two µl of cDNA and 5µl Lightcycler 480 probe master mix (Roche Cat # 04887301001) are added to 0.5µl of Human GAPDH TaqMan Probe (4326317E) and 0.5µl GRB14 Human probe (Hs00182949_m1, Thermo), or 0.5µl Cyno GAPDH (custom) and 0.5µl GRB14 Cyno probe per well in a 384 well plates (Roche cat # 04887301001). Real time PCR is done in a LightCycler480 Real Time PCR system (Roche). Each duplex is tested at least two times and data are normalized to cells transfected with a non-targeting control siRNA. To calculate relative fold change, real time data is analyzed using the ΔΔCt method and normalized to assays performed with cells transfected with a non-targeting control siRNA. The data are expressed as percent GRB14 mRNA remaining relative to control (e.g., GAPDH mRNA).

The results of a multi-dose screening assay in Hep3B cells are shown in Table 8. The results of a multi-dose free uptake assay in PCH cells are shown in Table 9. The results of a multi-dose free uptake assay in PHH cells are shown in Table 10. The results of IC50 assays in PCH and PHH cells are shown in Tables 11 and 12.

Table 8. Multi-dose *In vitro* Screening of GRB14 dsRNA agents in Hep3B Cells

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1947923.1	97	21	88	7	88	20
AD-1947924.1	68	3	98	11	93	27
AD-1947925.1	78	7	87	15	97	20
AD-1947926.1	67	11	76	14	94	18
AD-1947927.1	67	7	85	25	108	20
AD-1947928.1	90	13	86	14	95	15
AD-1947929.1	95	4	88	9	88	30
AD-1947930.1	86	11	79	19	86	10
AD-1947931.1	72	10	86	6	101	6
AD-1947932.1	77	8	102	16	93	13
AD-1947933.1	95	7	97	19	110	19
AD-1947934.1	77	9	98	8	96	5
AD-1947935.1	87	8	97	7	108	8
AD-1947936.1	89	9	94	5	107	4
AD-1947938.1	71	14	97	17	99	24
AD-1947939.1	46	13	82	9	88	16
AD-1947940.1	42	10	65	13	68	13
AD-1947941.1	51	5	66	7	74	16
AD-1947942.1	50	9	67	6	83	14
AD-1947943.1	60	7	79	6	87	10
AD-1947944.1	52	7	69	8	79	16
AD-1947945.1	67	11	74	5	88	19
AD-1947946.1	43	5	63	8	95	20
AD-1947947.1	62	5	73	15	79	9
AD-1947948.1	80	6	82	12	83	7
AD-1947949.1	84	11	81	11	72	3
AD-1947950.1	87	9	77	5	80	8
AD-1947951.1	74	11	79	16	83	9
AD-1947952.1	73	6	72	7	85	3
AD-1947953.1	85	8	96	8	86	29
AD-1947954.1	59	12	85	13	87	9
AD-1947955.1	71	5	81	6	79	23
AD-1947956.1	76	12	84	9	92	35
AD-1947957.1	70	7	80	3	99	3
AD-1947958.1	68	7	87	6	86	14
AD-1947959.1	83	4	84	10	88	5
AD-1947960.1	71	7	70	3	86	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1947961.1	52	6	70	8	92	9
AD-1947962.1	63	6	72	10	94	8
AD-1947963.1	76	13	72	5	80	12
AD-1947964.1	74	6	78	4	89	14
AD-1947965.1	77	4	96	8	105	22
AD-1947966.1	73	10	87	7	95	7
AD-1947967.1	86	5	95	13	102	9
AD-1947968.1	65	6	88	11	97	8
AD-1947969.1	52	11	99	5	95	16
AD-1947970.1	83	9	85	9	82	19
AD-1947971.1	76	10	81	13	85	16
AD-1947972.1	70	6	77	11	92	11
AD-1947973.1	82	5	84	10	86	12
AD-1947974.1	83	12	86	10	91	9
AD-1947975.1	74	8	77	6	83	16
AD-1947976.1	77	7	74	8	80	1
AD-1947977.1	86	9	91	8	95	7
AD-1947978.1	70	3	87	7	100	7
AD-1947979.1	54	4	67	10	85	5
AD-1947980.1	70	10	68	4	77	10
AD-1947981.1	90	11	87	5	92	6
AD-1947982.1	73	8	89	3	92	8
AD-1947983.1	87	7	70	8	85	2
AD-1947984.1	86	5	110	13	105	8
AD-1947985.1	88	3	100	8	106	6
AD-1947986.1	71	5	70	12	90	7
AD-1947987.1	86	12	85	8	91	7
AD-1947988.1	78	14	82	12	89	8
AD-1947989.1	70	10	83	2	89	5
AD-1947990.1	78	11	90	12	102	11
AD-1947991.1	82	8	95	4	104	8
AD-1947992.1	77	8	86	7	105	4
AD-1947993.1	63	5	83	4	108	10
AD-1947994.1	62	6	85	3	98	5
AD-1947995.1	75	6	98	6	112	4
AD-1947996.1	75	6	94	9	105	10
AD-1947997.1	94	5	88	9	104	7
AD-1947998.1	68	17	101	10	121	14
AD-1947999.1	71	10	84	12	92	16
AD-1948000.1	62	4	80	14	92	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948001.1	67	10	72	18	95	10
AD-1948002.1	68	7	70	7	91	8
AD-1948003.1	70	5	72	3	75	14
AD-1948004.1	47	5	62	6	79	8
AD-1948005.1	69	12	76	7	84	10
AD-1948006.1	61	3	75	9	81	12
AD-1948007.1	70	7	83	4	86	4
AD-1948008.1	63	7	79	3	99	5
AD-1948009.1	77	9	80	6	96	13
AD-1948010.1	64	5	77	10	84	3
AD-1948011.1	105	8	84	16	99	4
AD-1948012.1	96	9	101	7	100	12
AD-1948013.1	104	18	107	23	106	21
AD-1948014.1	72	8	78	8	85	5
AD-1948015.1	82	11	85	14	104	9
AD-1948016.1	71	2	77	11	78	4
AD-1948017.1	68	6	82	8	98	6
AD-1948018.1	55	19	81	9	93	12
AD-1948019.1	82	4	86	5	95	16
AD-1948020.1	74	8	79	6	91	7
AD-1948021.1	69	9	76	12	70	43
AD-1948022.1	48	7	76	2	87	6
AD-1948023.1	88	3	97	5	119	10
AD-1948024.1	70	6	88	2	90	2
AD-1948025.1	78	7	92	6	103	6
AD-1948026.1	73	12	84	14	98	8
AD-1948027.1	81	7	85	11	96	6
AD-1948028.1	80	3	93	8	96	8
AD-1948029.1	71	9	87	7	82	12
AD-1948030.1	103	15	91	9	88	8
AD-1948031.1	90	5	84	11	90	9
AD-1948032.1	68	7	82	8	93	8
AD-1948033.1	78	6	78	6	83	7
AD-1948034.1	60	6	70	17	94	4
AD-1948035.1	69	6	93	7	106	11
AD-1948036.1	62	4	71	7	76	6
AD-1948037.1	87	9	99	9	106	6
AD-1948038.1	60	12	71	8	81	7
AD-1948039.1	75	7	90	11	92	7
AD-1948040.1	67	5	82	4	81	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948041.1	80	10	98	8	107	7
AD-1948042.1	58	3	77	12	78	11
AD-1948043.1	76	11	94	7	95	13
AD-1948044.1	57	9	75	14	83	9
AD-1948045.1	66	12	75	5	89	12
AD-1948046.1	40	2	59	6	75	5
AD-1948047.1	68	5	87	7	106	12
AD-1948048.1	53	7	69	3	82	15
AD-1948049.1	87	5	83	6	106	5
AD-1948050.1	48	15	72	9	93	10
AD-1948051.1	73	8	98	4	107	32
AD-1948052.1	71	1	80	4	101	9
AD-1948053.1	85	11	114	6	110	32
AD-1948054.1	73	14	80	8	99	6
AD-1948055.1	86	6	97	8	110	9
AD-1948056.1	57	1	72	8	86	4
AD-1948057.1	104	16	132	14	139	16
AD-1948058.1	56	5	75	6	94	11
AD-1948059.1	73	4	89	5	107	5
AD-1948060.1	71	10	82	8	104	11
AD-1948061.1	66	5	69	11	82	26
AD-1948062.1	49	2	70	9	69	3
AD-1948063.1	70	3	83	6	90	5
AD-1948064.1	67	9	74	3	83	7
AD-1948065.1	95	7	92	12	91	4
AD-1948066.1	69	5	72	3	78	4
AD-1948067.1	78	9	103	6	114	4
AD-1948068.1	74	10	77	6	89	6
AD-1948069.1	79	6	91	13	96	7
AD-1948070.1	55	6	72	6	88	3
AD-1948071.1	47	4	75	6	113	5
AD-1948072.1	36	4	54	5	76	5
AD-1948073.1	47	1	62	2	79	11
AD-1948074.1	64	7	67	4	93	16
AD-1948075.1	50	6	58	4	92	8
AD-1948076.1	51	9	64	11	91	9
AD-1948077.1	51	9	70	12	101	15
AD-1948078.1	39	6	58	3	83	9
AD-1948079.1	55	6	84	6	114	8
AD-1948080.1	45	4	65	2	97	1

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948081.1	55	11	71	5	103	3
AD-1948082.1	38	3	50	2	71	1
AD-1948083.1	57	8	62	6		11
AD-1948084.1	44	6	53	6	79	9
AD-1948085.1	59	7	74	4	79	53
AD-1948086.1	60	11	84	3	101	4
AD-1948087.1	73	4	95	5	122	17
AD-1948088.1	39	3	44	3	64	5
AD-1948089.1	48	5	70	3	96	4
AD-1948090.1	45	3	66	5	95	8
AD-1948091.1	48	3	60	4	85	6
AD-1948092.1	46	3	53	7	78	13
AD-1948093.1	35	18	84	8	108	11
AD-1948094.1	66	3	53	6	68	6
AD-1948095.1	56	16	61	5	73	11
AD-1948096.1	41	6	68	7	75	19
AD-1948097.1	48	3	64	7	73	2
AD-1948098.1	34	5	54	5	70	6
AD-1948099.1	40	3	54	8	75	7
AD-1948100.1	41	3	52	4	68	4
AD-1948101.1	43	1	69	5	112	13
AD-1948102.1	39	4	56	3	82	4
AD-1948103.1	40	12	65	2	80	24
AD-1948104.1	40	2	49	1	71	4
AD-1948105.1	58	6	65	4	93	9
AD-1948106.1	40	8	55	4	83	14
AD-1948107.1	64	7	84	9	104	5
AD-1948108.1	59	6	68	9	91	11
AD-1948109.1	56	5	81	5	117	6
AD-1948110.1	38	8	53	1	72	10
AD-1948111.1	38	3	71	7	112	9
AD-1948112.1	40	5	63	6	87	12
AD-1948113.1	37	6	61	6	104	7
AD-1948114.1	36	5	49	3	78	11
AD-1948115.1	50	1	65	4	88	12
AD-1948116.1	45	7	64	1	86	8
AD-1948117.1	51	2	76	0	107	10
AD-1948118.1	50	6	53	5	74	12
AD-1948119.1	75	13	84	3	109	7
AD-1948120.1	43	7	51	3	74	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948121.1	63	4	73	5	99	7
AD-1948122.1	43	5	55	12	80	4
AD-1948123.1	62	8	64	8	88	8
AD-1948124.1	43	4	65	10	79	26
AD-1948125.1	67	6	85	2	91	4
AD-1948126.1	55	4	57	4	81	11
AD-1948127.1	35	2	49	5	73	5
AD-1948128.1	57	9	64	4	84	14
AD-1948129.1	40	9	52	4	76	13
AD-1948130.1	39	13	58	2	75	7
AD-1948131.1	35	3	47	3	61	3
AD-1948132.1	49	3	65	5	95	6
AD-1948133.1	43	3	50	8	69	6
AD-1948134.1	45	5	59	8	73	12
AD-1948135.1	45	3	73	16	89	8
AD-1948136.1	95	11	113	10	124	7
AD-1948137.1	46	5	48	6	70	4
AD-1948138.1	67	11	88	14	107	16
AD-1948139.1	61	3	59	9	82	23
AD-1948140.1	46	7	52	5	83	7
AD-1948141.1	48	5	63	6	81	6
AD-1948142.1	37	3	48	3	71	6
AD-1948143.1	56	13	68	7	106	8
AD-1948144.1	64	7	72	7	92	9
AD-1948145.1	60	6	87	8	124	5
AD-1948146.1	48	4	58	4	84	5
AD-1948147.1	62	4	88	12	120	9
AD-1948148.1	49	5	64	12	91	5
AD-1948149.1	49	5	60	4	91	2
AD-1948150.1	54	3	81	13	98	6
AD-1948151.1	61	6	72	7	114	6
AD-1948152.1	47	4	53	4	81	7
AD-1948153.1	50	0	60	3	89	13
AD-1948154.1	37	5	49	2	89	6
AD-1948155.1	55	7	86	11	99	12
AD-1948156.1	48	3	43	4	66	5
AD-1948157.1	51	7	73	8	98	11
AD-1948158.1	41	5	45	11	74	1
AD-1948159.1	48	3	65	7	94	8
AD-1948160.1	33	5	45	1	63	4

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948161.1	45	11	58	6	75	4
AD-1948162.1	39	3	46	3	65	3
AD-1948163.1	39	4	58	8	67	4
AD-1948164.1	38	7	45	5	57	2
AD-1948165.1	51	7	61	5	77	2
AD-1948166.1	42	3	47	7	66	7
AD-1948167.1	48	2	58	4	85	5
AD-1948168.1	46	8	51	4	74	7
AD-1948169.1	43	2	51	7	71	3
AD-1948170.1	46	8	54	3	80	10
AD-1948171.1	95	9	118	18	143	8
AD-1948172.1	28	2	49	4	79	7
AD-1948173.1	54	6	60	10	93	5
AD-1948174.1	40	7	43	7	63	3
AD-1948175.1	54	6	69	11	97	6
AD-1948176.1	48	3	70	8	90	5
AD-1948177.1	76	8	80	10	114	10
AD-1948178.1	43	2	47	2	66	5
AD-1948179.1	59	11	69	4	100	10
AD-1948180.1	34	4	45	3	72	3
AD-1948181.1	48	1	72	13	99	9
AD-1948182.1	44	6	58	8	82	7
AD-1948183.1	63	6	72	6	111	7
AD-1948184.1	40	3	54	2	74	4
AD-1948185.1	58	5	74	8	102	15
AD-1948186.1	91	6	68	4	79	10
AD-1948187.1	44	7	58	11	84	12
AD-1948188.1	41	4	49	1	76	6
AD-1948189.1	44	5	61	7	90	6
AD-1948190.1	39	9	54	5	75	5
AD-1948191.1	49	4	60	3	95	5
AD-1948192.1	40	1	57	3	76	4
AD-1948193.1	52	3	74	7	104	9
AD-1948194.1	43	8	58	4	70	22
AD-1948195.1	60	3	73	12	107	8
AD-1948196.1	27	4	38	4	53	2
AD-1948197.1	78	9	57	8	72	7
AD-1948198.1	40	2	69	4	82	5
AD-1948199.1	31	2	44	3	69	3
AD-1948200.1	17	2	30	4	48	2

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948201.1	26	3	48	5	75	6
AD-1948202.1	25	1	38	4	54	7
AD-1948203.1	30	6	54	4	68	4
AD-1948204.1	43	6	65	2	90	10
AD-1948205.1	33	3	48	8	70	5
AD-1948206.1	32	3	38	5	54	9
AD-1948207.1	44	2	50	6	68	9
AD-1948208.1	27	4	34	3	44	4
AD-1948209.1	37	2	50	7	74	9
AD-1948210.1	28	2	41	3	64	6
AD-1948211.1	57	7	88	7	129	8
AD-1948212.1	28	2	49	7	65	6
AD-1948213.1	56	8	96	12	119	8
AD-1948214.1	36	4	60	5	81	8
AD-1948215.1	92	10	116	8	119	6
AD-1948216.1	59	5	82	11	99	12
AD-1948217.1	78	10	110	16	101	19
AD-1948218.1	32	6	42	10	69	13
AD-1948219.1	55	6	73	4	81	25
AD-1948220.1	30	6	35	5	51	4
AD-1948221.1	49	4	52	8	76	9
AD-1948222.1	34	5	41	4	58	6
AD-1948223.1	37	5	44	1	62	8
AD-1948224.1	29	4	41	5	53	1
AD-1948225.1	31	4	48	5	72	3
AD-1948226.1	26	3	41	8	51	4
AD-1948227.1	40	4	49	3	70	4
AD-1948228.1	36	3	42	3	58	5
AD-1948229.1	48	4	53	9	69	5
AD-1948230.1	45	5	53	3	73	7
AD-1948231.1	53	4	60	8	89	13
AD-1948232.1	36	2	39	3	64	12
AD-1948233.1	62	7	61	5	95	17
AD-1948234.1	32	4	41	3	56	9
AD-1948235.1	65	4	63	4	88	9
AD-1948236.1	33	5	43	2	57	3
AD-1948237.1	52	6	55	10	83	11
AD-1948238.1	34	3	43	4	51	11
AD-1948239.1	43	4	57	8	87	4
AD-1948240.1	31	4	45	3	72	5

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948241.1	36	6	62	5	112	11
AD-1948242.1	22	3	42	2	65	4
AD-1948243.1	14	2	43	2	77	7
AD-1948244.1	63	12	85	8	93	3
AD-1948245.1	25	2	52	7	82	7
AD-1948246.1	24	3	42	3	71	11
AD-1948247.1	30	8	48	8	75	16
AD-1948248.1	24	3	34	6	46	15
AD-1948249.1	36	4	54	6	80	13
AD-1948250.1	26	4	39	7	53	13
AD-1948251.1	66	9	87	15	101	9
AD-1948252.1	22	3	36	4	47	7
AD-1948253.1	20	2	38	4	64	5
AD-1948254.1	18	5	35	5	43	5
AD-1948255.1	25	3	43	5	67	5
AD-1948256.1	28	4	43	3	63	9
AD-1948257.1	24	3	45	5	70	7
AD-1948258.1	26	4	39	5	59	13
AD-1948259.1	47	2	49	7	76	5
AD-1948260.1	30	2	39	6	62	4
AD-1948261.1	36	5	53	7	89	11
AD-1948262.1	31	6	43	5	69	8
AD-1948263.1	26	5	63	9	90	23
AD-1948264.1	28	2	48	8	63	13
AD-1948265.1	57	6	58	7	105	3
AD-1948266.1	29	2	54	4	75	10
AD-1948267.1	52	1	85	6	122	9
AD-1948268.1	21	3	40	5	62	9
AD-1948269.1	37	1	58	2	98	6
AD-1948270.1	24	4	42	4	55	5
AD-1948271.1	51	6	65	3	104	11
AD-1948272.1	25	4	38	2	68	8
AD-1948273.1	56	2	71	3	108	9
AD-1948274.1	28	5	42	4	69	6
AD-1948275.1	31	3	56	6	81	9
AD-1948276.1	29	5	34	7	46	15
AD-1948277.1	66	7	87	3	129	5
AD-1948278.1	33	7	40	4	60	10
AD-1948279.1	32	2	42	8	59	8
AD-1948280.1	27	4	37	4	56	9

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948281.1	41	3	44	4	73	13
AD-1948282.1	29	2	31	3	55	14
AD-1948283.1	44	8	60	10	96	16
AD-1948284.1	17	5	32	5	50	4
AD-1948285.1	16	3	35	3	62	6
AD-1948286.1	27	5	37	10	53	5
AD-1948287.1	29	4	49	3	86	15
AD-1948288.1	16	5	29	2	47	9
AD-1948289.1	34	5	53	2	77	6
AD-1948290.1	11	3	29	6	43	6
AD-1948291.1	27	3	46	7	77	8
AD-1948292.1	28	3	35	3	51	8
AD-1948293.1	25	2	42	5	76	10
AD-1948294.1	46	7	65	13	77	19
AD-1948295.1	37	6	59	16	99	29
AD-1948296.1	13	4	33	7	53	7
AD-1948297.1	28	2	37	6	55	7
AD-1948298.1	33	3	37	4	57	5
AD-1948299.1	47	3	44	7	67	18
AD-1948300.1	55	5	59	7	94	4
AD-1948301.1	22	3	32	5	54	7
AD-1948302.1	19	2	31	11	50	3
AD-1948303.1	18	2	30	9	50	6
AD-1948304.1	31	2	34	6	51	6
AD-1948305.1	25	4	39	6	75	2
AD-1948306.1	27	1	35	5	60	6
AD-1948307.1	43	3	54	13	71	12
AD-1948308.1	36	4	43	4	65	5
AD-1948309.1	46	8	56	4	82	3
AD-1948310.1	29	9	49	9	82	13
AD-1948311.1	30	6	43	5	61	19
AD-1948312.1	56	11	73	15	95	8
AD-1948313.1	38	1	42	8	73	4
AD-1948314.1	30	1	46	14	79	9
AD-1948315.1	32	1	39	8	62	8
AD-1948316.1	46	3	46	7	59	11
AD-1948317.1	41	6	44	6	66	12
AD-1948318.1	45	4	52	9	73	8
AD-1948319.1	37	5	40	5	68	6
AD-1948320.1	45	5	41	2	62	2

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948321.1	29	2	39	10	60	7
AD-1948322.1	32	1	43	8	66	5
AD-1948323.1	37	5	40	7	52	5
AD-1948324.1	59	6	62	12	81	10
AD-1948325.1	91	14	89	13	118	21
AD-1948326.1	42	10	39	10	70	8
AD-1948327.1	37	3	47	8	74	8
AD-1948328.1	35	3	47	9	81	18
AD-1948329.1	41	3	42	3	73	12
AD-1948330.1	72	8	76	5	96	7
AD-1948331.1	36	4	43	5	66	13
AD-1948332.1	31	3	40	12	62	10
AD-1948333.1	45	3	57	8	85	5
AD-1948334.1	36	3	43	8	69	5
AD-1948335.1	40	5	45	10	66	9
AD-1948336.1	28	4	32	11	63	15
AD-1948337.1	44	7	52	10	84	11
AD-1948338.1	18	4	37	5	56	3
AD-1948339.1	23	3	37	5	62	4
AD-1948340.1	18	3	33	7	62	12
AD-1948341.1	17	3	27	6	71	13
AD-1948342.1	31	5	43	11	78	19
AD-1948343.1	25	5	42	11	75	9
AD-1948344.1	45	6	56	5	86	7
AD-1948345.1	17	2	28	8	53	12
AD-1948346.1	11	2	26	5	52	4
AD-1948347.1	42	4	45	6	58	14
AD-1948348.1	83	5	88	13	99	4
AD-1948349.1	40	2	46	4	73	12
AD-1948350.1	33	1	40	6	57	7
AD-1948351.1	36	3	41	3	62	8
AD-1948352.1	54	3	69	5	98	5
AD-1948353.1	44	2	47	5	75	10
AD-1948354.1	34	3	35	4	48	7
AD-1948355.1	58	4	77	10	92	5
AD-1948356.1	33	4	41	6	44	4
AD-1948357.1	43	3	49	5	66	12
AD-1948358.1	37	3	43	3	51	6
AD-1948359.1	46	5	49	4	59	3
AD-1948360.1	40	1	47	4	61	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948361.1	51	3	58	7	80	11
AD-1948362.1	32	5	40	4	47	3
AD-1948363.1	42	6	47	4	60	7
AD-1948364.1	31	2	38	4	47	6
AD-1948365.1	42	6	51	4	68	9
AD-1948366.1	31	3	40	5	73	17
AD-1948367.1	40	2	57	16	93	15
AD-1948368.1	36	3	41	4	59	15
AD-1948369.1	67	8	70	6	121	22
AD-1948370.1	27	3	34	4	54	5
AD-1948371.1	60	15	54	3	88	10
AD-1948372.1	39	6	43	6	59	9
AD-1948373.1	39	2	44	3	62	5
AD-1948374.1	31	5	37	6	51	11
AD-1948375.1	28	2	41	4	57	10
AD-1948376.1	25	2	39	9	62	11
AD-1948377.1	30	3	41	3	52	7
AD-1948378.1	19	3	33	6	55	12
AD-1948379.1	27	1	39	3	56	13
AD-1948380.1	26	3	36	3	57	13
AD-1948381.1	25	1	40	8	60	10
AD-1948382.1	33	2	42	5	59	6
AD-1948383.1	44	3	46	5	69	13
AD-1948384.1	41	2	39	7	51	8
AD-1948385.1	35	1	39	5	75	9
AD-1948386.1	34	2	37	4	55	4
AD-1948387.1	94	13	69	11	66	9
AD-1948388.1	36	2	44	6	73	16
AD-1948389.1	33	3	45	7	76	10
AD-1948390.1	23	4	36	1	60	7
AD-1948391.1	28	1	43	7	65	6
AD-1948392.1	30	5	42	4	70	3
AD-1948393.1	40	4	58	6	98	21
AD-1948394.1	29	2	36	7	59	9
AD-1948395.1	26	2	37	5	73	11
AD-1948396.1	24	3	38	6	69	9
AD-1948397.1	40	3	51	7	80	17
AD-1948398.1	23	2	33	5	53	10
AD-1948399.1	32	3	40	7	66	5
AD-1948400.1	31	2	35	6	72	13

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948401.1	30	3	42	9	64	11
AD-1948402.1	37	3	47	7	75	9
AD-1948403.1	34	3	47	9	69	7
AD-1948404.1	22	1	30	5	60	12
AD-1948405.1	20	2	34	7	51	11
AD-1948406.1	28	1	31	7	46	6
AD-1948407.1	31	2	36	1	53	6
AD-1948408.1	28	2	33	6	51	8
AD-1948409.1	30	2	42	9	72	14
AD-1948410.1	22	3	31	5	44	7
AD-1948411.1	34	6	41	4	55	10
AD-1948412.1	16	3	28	5	45	8
AD-1948413.1	42	3	49	4	74	11
AD-1948414.1	39	4	49	9	75	8
AD-1948415.1	40	3	45	8	61	14
AD-1948416.1	40	5	47	6	66	13
AD-1948417.1	44	10	51	2	102	5
AD-1948418.1	34	6	40	4	78	7
AD-1948419.1	31	11	46	13	75	4
AD-1948420.1	32	2	38	5	55	5
AD-1948421.1	36	4	45	7	68	9
AD-1948422.1	40	4	55	8	89	5
AD-1948423.1	35	3	53	5	73	16
AD-1948424.1	32	2	38	7	52	6
AD-1948425.1	50	3	57	3	79	18
AD-1948426.1	30	4	36	4	60	14
AD-1948427.1	49	1	68	10	106	11
AD-1948428.1	43	2	44	4	61	8
AD-1948429.1	47	4	54	10	82	5
AD-1948430.1	32	5	36	3	47	6
AD-1948431.1	31	2	44	4	56	8
AD-1948432.1	29	2	34	3	52	9
AD-1948433.1	34	11	48	6	51	13
AD-1948434.1	32	7	41	7	57	10
AD-1948435.1	36	4	42	3	55	4
AD-1948436.1	34	5	39	4	53	10
AD-1948437.1	44	6	49	4	63	7
AD-1948438.1	33	2	41	8	51	9
AD-1948439.1	50	2	56	10	76	5
AD-1948440.1	40	6	39	2	50	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948441.1	54	6	58	3	64	8
AD-1948442.1	35	2	43	4	56	9
AD-1948443.1	40	15	56	11	84	12
AD-1948444.1	37	4	42	9	55	11
AD-1948445.1	46	5	54	5	69	10
AD-1948446.1	43	2	42	4	56	10
AD-1948447.1	52	11	50	8	64	13
AD-1948448.1	73	4	73	11	85	5
AD-1948449.1	49	4	63	7	93	27
AD-1948450.1	43	7	40	14	72	6
AD-1948451.1	42	6	64	12	98	14
AD-1948452.1	32	6	39	12	77	12
AD-1948453.1	40	3	65	12	103	19
AD-1948454.1	31	3	45	8	69	10
AD-1948455.1	51	4	60	4	85	11
AD-1948456.1	34	8	46	8	73	13
AD-1948457.1	49	5	57	3	87	10
AD-1948458.1	49	6	56	5	89	12
AD-1948459.1	57	5	62	6	84	11
AD-1948460.1	34	3	37	4	58	12
AD-1948461.1	48	3	63	12	82	17
AD-1948462.1	35	4	41	4	61	15
AD-1948463.1	50	3	68	10	105	10
AD-1948464.1	48	5	60	6	80	9
AD-1948465.1	47	5	60	5	83	29
AD-1948466.1	36	9	67	16	80	13
AD-1948467.1	44	3	52	9	82	5
AD-1948468.1	44	8	48	8	77	0
AD-1948469.1	70	8	89	12	109	4
AD-1948470.1	54	10	89	9	95	11
AD-1948471.1	49	4	64	12	105	3
AD-1948472.1	45	3	51	8	72	10
AD-1948473.1	47	7	63	8	99	7
AD-1948474.1	30	2	43	8	75	11
AD-1948475.1	61	9	64	8	92	9
AD-1948476.1	45	2	59	7	84	3
AD-1948477.1	46	5	53	6	77	11
AD-1948478.1	35	3	40	5	61	11
AD-1948479.1	42	6	50	5	79	11
AD-1948480.1	34	6	43	5	65	12

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948481.1	45	4	51	19	87	32
AD-1948482.1	40	3	46	17	76	17
AD-1948483.1	57	1	60	6	94	17
AD-1948484.1	40	6	48	8	86	23
AD-1948485.1	57	2	70	5	98	17
AD-1948486.1	42	1	47	4	61	14
AD-1948487.1	51	2	64	8	85	10
AD-1948488.1	43	4	45	5	60	6
AD-1948489.1	75	5	87	10	134	20
AD-1948490.1	53	3	66	4	97	11
AD-1948491.1	123	19	132	2	135	3
AD-1948492.1	44	2	47	4	64	8
AD-1948493.1	42	3	55	5	71	11
AD-1948494.1	35	2	46	6	50	11
AD-1948495.1	50	8	47	2	68	12
AD-1948496.1	38	8	41	11	70	10
AD-1948497.1	31	9	38	10	52	9
AD-1948498.1	40	5	40	8	56	12
AD-1948499.1	32	5	38	10	46	10
AD-1948500.1	53	3	53	4	69	8
AD-1948501.1	34	11	40	10	56	10
AD-1948502.1	38	2	45	5	53	8
AD-1948503.1	31	2	32	7	52	5
AD-1948504.1	42	6	50	1	70	12
AD-1948505.1	42	1	59	6	86	10
AD-1948506.1	77	9	86	8	107	7
AD-1948507.1	39	3	43	4	71	8
AD-1948508.1	59	8	57	3	85	4
AD-1948509.1	35	3	40	4	66	8
AD-1948510.1	55	8	55	9	75	10
AD-1948511.1	55	6	52	18	79	7
AD-1948512.1	42	5	49	11	79	5
AD-1948513.1	89	8	94	12	104	35
AD-1948514.1	42	2	56	5	81	16
AD-1948515.1	74	8	108	9	123	13
AD-1948516.1	33	4	47	9	82	6
AD-1948517.1	38	4	56	8	90	13
AD-1948518.1	33	8	49	4	86	8
AD-1948519.1	46	4	58	7	94	11
AD-1948520.1	29	4	39	5	59	7

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948521.1	42	6	53	7	75	11
AD-1948522.1	34	3	46	5	75	6
AD-1948523.1	46	4	57	3	88	12
AD-1948524.1	34	1	41	8	52	8
AD-1948525.1	28	4	38	6	72	12
AD-1948526.1	28	3	33	4	58	9
AD-1948527.1	31	8	45	10	65	10
AD-1948528.1	32	2	35	4	52	7
AD-1948529.1	38	5	41	9	57	8
AD-1948530.1	26	2	33	7	64	17
AD-1948531.1	18	2	32	7	52	4
AD-1948532.1	20	2	28	6	49	6
AD-1948533.1	17	1	30	7	53	6
AD-1948534.1	55	3	65	11	84	5
AD-1948535.1	40	6	51	7	77	5
AD-1948536.1	52	5	70	8	93	9
AD-1948537.1	29	3	42	4	70	12
AD-1948538.1	22	1	35	6	62	13
AD-1948539.1	42	3	46	5	57	7
AD-1948540.1	30	2	38	3	61	9
AD-1948541.1	35	2	48	14	66	7
AD-1948542.1	31	8	40	5	64	4
AD-1948543.1	46	6	60	7	87	11
AD-1948544.1	29	2	37	7	70	16
AD-1948545.1	48	5	62	10	90	15
AD-1948546.1	21	1	30	3	57	10
AD-1948547.1	37	2	48	4	64	11
AD-1948548.1	39	4	49	7	79	7
AD-1948549.1	50	3	54	8	82	11
AD-1948550.1	45	3	53	6	78	9
AD-1948551.1	54	2	61	8	77	13
AD-1948552.1	38	1	45	4	57	5
AD-1948553.1	94	4	101	5	124	9
AD-1948554.1	34	3	34	1	52	8
AD-1948555.1	46	3	47	10	61	12
AD-1948556.1	32	1	45	3	72	9
AD-1948557.1	50	1	47	2	67	9
AD-1948558.1	44	10	48	8	67	11
AD-1948559.1	60	6	65	20	86	16
AD-1948560.1	49	4	53	12	81	7

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948561.1	37	3	45	11	67	8
AD-1948562.1	38	3	39	3	56	9
AD-1948563.1	45	2	44	5	56	10
AD-1948564.1	31	2	36	3	48	8
AD-1948565.1	37	2	41	5	50	6
AD-1948566.1	32	5	35	4	48	6
AD-1948567.1	38	5	45	3	59	15
AD-1948568.1	36	1	40	3	63	14
AD-1948569.1	50	3	74	18	101	6
AD-1948570.1	28	2	34	3	56	13
AD-1948571.1	40	5	49	5	73	14
AD-1948572.1	23	3	32	6	44	7
AD-1948573.1	34	2	39	7	67	7
AD-1948574.1	35	5	46	7	72	10
AD-1948575.1	46	1	51	6	85	14
AD-1948576.1	34	5	41	4	69	7
AD-1948577.1	45	6	48	4	76	8
AD-1948578.1	31	4	38	3	62	9
AD-1948579.1	47	5	61	6	99	13
AD-1948580.1	33	4	42	11	73	6
AD-1948581.1	46	3	54	8	96	12
AD-1948582.1	33	1	45	9	73	9
AD-1948583.1	57	7	81	3	122	7
AD-1948584.1	25	3	31	3	51	11
AD-1948585.1	29	4	42	9	73	15
AD-1948586.1	25	3	30	4	44	8
AD-1948587.1	47	3	47	4	56	6
AD-1948588.1	33	3	39	6	49	5
AD-1948589.1	31	4	38	7	49	3
AD-1948590.1	25	0	29	3	40	7
AD-1948591.1	30	3	33	3	46	3
AD-1948592.1	30	3	31	3	49	8
AD-1948593.1	31	4	42	3	72	8
AD-1948594.1	22	3	27	3	40	8
AD-1948595.1	33	2	39	7	54	6
AD-1948596.1	21	2	34	5	55	10
AD-1948597.1	45	6	62	6	94	5
AD-1948598.1	23	2	34	3	45	10
AD-1948599.1	39	2	41	5	57	7
AD-1948600.1	34	4	38	6	62	9

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948601.1	32	3	36	3	59	5
AD-1948602.1	31	3	34	6	64	11
AD-1948603.1	52	10	61	14	87	7
AD-1948604.1	33	5	36	6	58	11
AD-1948605.1	56	8	58	4	84	7
AD-1948606.1	37	3	39	6	64	6
AD-1948607.1	45	1	53	10	88	16
AD-1948608.1	27	5	35	5	64	4
AD-1948609.1	48	4	53	4	85	15
AD-1948610.1	36	4	34	5	48	9
AD-1948611.1	52	1	54	7	84	12
AD-1948612.1	36	2	38	4	48	13
AD-1948613.1	50	3	61	8	93	12
AD-1948614.1	29	3	33	3	51	10
AD-1948615.1	56	6	63	5	84	11
AD-1948616.1	42	2	41	5	66	9
AD-1948617.1	61	3	54	5	85	9
AD-1948618.1	33	6	34	4	52	12
AD-1948619.1	46	3	52	6	59	16
AD-1948620.1	34	4	41	8	49	10
AD-1948621.1	54	4	50	6	64	12
AD-1948622.1	32	8	34	5	54	6
AD-1948623.1	60	7	69	10	82	22
AD-1948624.1	33	5	37	7	55	8
AD-1948625.1	42	3	39	2	61	9
AD-1948626.1	33	4	36	7	55	8
AD-1948627.1	33	2	39	7	52	11
AD-1948628.1	30	1	34	8	50	10
AD-1948629.1	29	4	39	8	68	10
AD-1948630.1	32	4	41	6	66	9
AD-1948631.1	29	1	41	7	60	13
AD-1948632.1	29	3	31	4	48	8
AD-1948633.1	32	2	33	3	51	3
AD-1948634.1	30	2	32	4	53	8
AD-1948636.1	33	9	40	8	61	4
AD-1948637.1	43	9	50	4	67	10
AD-1948638.1	22	4	29	5	48	12
AD-1948639.1	35	6	49	4	71	13
AD-1948640.1	23	3	28	5	37	7
AD-1948641.1	44	5	50	7	60	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948642.1	26	3	31	6	44	8
AD-1948643.1	38	3	44	8	61	14
AD-1948644.1	31	4	32	3	49	11
AD-1948645.1	39	5	45	9	62	7
AD-1948646.1	16	1	21	3	39	10
AD-1948647.1	21	2	31	5	53	9
AD-1948648.1	21	2	26	6	45	6
AD-1948649.1	39	3	44	4	65	7
AD-1948650.1	28	2	30	3	40	9
AD-1948651.1	41	5	41	3	56	2
AD-1948652.1	30	5	38	5	54	8
AD-1948653.1	37	5	47	5	73	11
AD-1948654.1	30	5	35	2	56	11
AD-1948655.1	38	2	38	6	65	7
AD-1948656.1	36	4	31	2	49	15
AD-1948657.1	33	2	38	6	58	12
AD-1948658.1	61	6	66	10	73	4
AD-1948659.1	44	6	57	6	81	5
AD-1948660.1	78	5	79	10	76	6
AD-1948661.1	71	8	58	5	63	6
AD-1948662.1	47	6	41	6	60	10
AD-1948663.1	83	5	81	8	101	17
AD-1948664.1	26	5	38	6	67	11
AD-1948666.1	57	2	67	16	85	7
AD-1948667.1	40	10	51	10	72	9
AD-1948668.1	47	10	58	6	76	10
AD-1948670.1	49	9	94	5	98	19
AD-1948671.1	63	9	61	9	110	22
AD-1948672.1	103	10	66	7	66	8
AD-1948673.1	37	5	41	12	61	8
AD-1948674.1	30	6	44	6	68	8
AD-1948675.1	46	7	55	8	79	4
AD-1948676.1	30	5	42	5	61	10
AD-1948677.1	33	8	45	8	68	12
AD-1948678.1	28	5	45	5	64	7
AD-1948679.1	31	4	42	3	53	9
AD-1948680.1	42	2	42	4	53	12
AD-1948681.1	39	7	44	3	64	6
AD-1948682.1	24	7	39	4	48	10
AD-1948683.1	27	9	40	5	49	9

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948684.1	27	2	37	2	50	11
AD-1948685.1	24	6	32	5	47	8
AD-1948686.1	36	5	49	5	65	8
AD-1948687.1	31	4	40	1	57	6
AD-1948688.1	34	7	38	5	58	8
AD-1948689.1	41	5	48	3	70	10
AD-1948690.1	43	4	54	4	68	8
AD-1948691.1	52	11	64	6	82	10
AD-1948692.1	40	4	44	7	63	12
AD-1948693.1	35	7	45	2	59	10
AD-1948694.1	37	3	43	4	59	6
AD-1948695.1	34	6	45	1	58	8
AD-1948696.1	36	4	46	6	67	6
AD-1948697.1	54	10	51	7	66	4
AD-1948699.1	58	11	59	6	82	10
AD-1948700.1	37	4	40	4	59	9
AD-1948701.1	35	7	40	7	75	7
AD-1948702.1	36	7	46	4	62	12
AD-1948703.1	39	4	43	4	58	12
AD-1948704.1	35	6	41	4	53	11
AD-1948705.1	44	5	49	6	59	10
AD-1948706.1	46	5	58	9	94	8
AD-1948707.1	39	7	44	4	54	5
AD-1948708.1	34	3	43	6	62	6
AD-1948709.1	54	9	76	15	101	6
AD-1948710.1	37	5	46	5	61	4
AD-1948711.1	47	6	48	4	70	8
AD-1948712.1	39	4	44	2	54	6
AD-1948713.1	43	5	42	6	52	10
AD-1948714.1	35	8	46	9	61	8
AD-1948715.1	42	6	47	3	58	10
AD-1948716.1	35	4	50	6	72	11
AD-1948717.1	42	6	43	6	57	4
AD-1948718.1	43	5	45	3	68	7
AD-1948719.1	55	4	48	10	55	4
AD-1948720.1	45	5	48	4	59	10
AD-1948721.1	46	6	48	4	65	10
AD-1948722.1	49	4	49	3	66	8
AD-1948723.1	41	4	50	6	67	4
AD-1948724.1	29	6	40	7	63	3

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948725.1	38	4	44	7	72	9
AD-1948726.1	30	3	44	9	70	9
AD-1948727.1	35	7	44	0	66	7
AD-1948728.1	32	3	42	5	60	7
AD-1948729.1	43	7	54	7	80	12
AD-1948730.1	45	7	47	3	62	7
AD-1948731.1	46	7	51	3	61	3
AD-1948732.1	37	5	42	4	60	12
AD-1948733.1	43	7	53	8	74	8
AD-1948734.1	35	6	43	7	55	10
AD-1948735.1	47	6	57	7	75	8
AD-1948736.1	48	6	51	6	69	7
AD-1948737.1	63	7	63	3	73	10
AD-1948738.1	52	2	60	1	80	9
AD-1948739.1	47	4	52	5	66	8
AD-1948740.1	39	4	49	7	62	5
AD-1948741.1	44	3	54	8	79	12
AD-1948742.1	45	9	47	6	62	8
AD-1948743.1	30	4	42	2	61	8
AD-1948744.1	36	5	46	3	65	12
AD-1948745.1	34	7	44	5	61	9
AD-1948746.1	34	7	48	6	63	7
AD-1948747.1	31	6	44	7	57	7
AD-1948748.1	29	4	40	4	53	8
AD-1948750.1	35	5	42	1	58	4
AD-1948751.1	44	6	49	6	67	8
AD-1948752.1	35	4	43	2	60	5
AD-1948753.1	38	3	46	5	59	7
AD-1948754.1	36	4	48	8	70	5
AD-1948755.1	43	8	57	8	83	9
AD-1948756.1	42	3	53	8	72	13
AD-1948757.1	49	4	65	9	92	8
AD-1948758.1	30	5	41	3	53	9
AD-1948759.1	42	6	58	7	87	13
AD-1948760.1	29	3	42	7	56	9
AD-1948762.1	29	4	40	4	54	8
AD-1948763.1	62	11	77	7	103	4
AD-1948764.1	34	5	53	10	78	6
AD-1948765.1	32	4	46	8	64	7
AD-1948766.1	36	6	49	4	73	6

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948767.1	47	6	58	6	72	11
AD-1948768.1	39	7	46	6	66	3
AD-1948769.1	46	8	59	8	91	6
AD-1948770.1	34	6	41	4	55	7
AD-1948771.1	34	7	45	5	57	10
AD-1948772.1	41	7	55	6	77	13
AD-1948773.1	44	6	44	8	59	9
AD-1948774.1	31	4	39	3	47	6
AD-1948775.1	26	4	36	4	49	8
AD-1948776.1	32	3	38	5	51	8
AD-1948777.1	31	7	44	1	61	9
AD-1948778.1	39	6	58	6	77	7
AD-1948779.1	33	5	43	5	53	7
AD-1948780.1	30	2	42	4	56	6
AD-1948781.1	33	5	46	6	56	7
AD-1948782.1	30	6	41	6	62	5
AD-1948783.1	40	5	46	7	59	9
AD-1948784.1	44	10	56	4	81	8
AD-1948785.1	31	4	45	8	59	8
AD-1948786.1	28	4	38	5	48	7
AD-1948787.1	41	5	51	7	67	5
AD-1948788.1	41	9	43	2	54	3
AD-1948789.1	55	10	43	9	61	6
AD-1948790.1	42	4	43	6	62	9
AD-1948791.1	39	5	41	7	58	8
AD-1948792.1	37	4	40	9	71	8
AD-1948793.1	41	3	50	7	65	9
AD-1948794.1	44	5	51	4	75	9
AD-1948795.1	44	7	58	6	79	9
AD-1948796.1	42	6	49	2	69	11
AD-1948797.1	45	5	51	6	71	7
AD-1948798.1	40	7	44	5	54	9
AD-1948799.1	38	10	52	5	66	2
AD-1948800.1	32	10	39	5	55	7
AD-1948801.1	41	10	53	10	88	10
AD-1948802.1	60	11	75	5	91	8
AD-1948803.1	39	7	46	4	68	10
AD-1948804.1	46	8	64	10	86	9
AD-1948805.1	44	3	43	11	47	6
AD-1948806.1	36	7	44	4	61	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948807.1	43	4	42	7	46	4
AD-1948808.1	62	8	68	8	78	2
AD-1948809.1	42	4	42	9	55	7
AD-1948810.1	42	3	50	7	68	5
AD-1948811.1	33	4	41	7	56	6
AD-1948812.1	28	5	37	4	57	8
AD-1948813.1	37	9	53	6	78	8
AD-1948814.1	55	8	72	6	89	7
AD-1948815.1	36	7	45	4	61	7
AD-1948816.1	25	5	38	5	56	3
AD-1948817.1	40	4	50	4	75	7
AD-1948818.1	27	5	41	3	65	5
AD-1948819.1	31	6	44	5	71	2
AD-1948820.1	37	7	39	5	52	6
AD-1948821.1	52	10	53	6	59	13
AD-1948822.1	36	4	49	11	68	12
AD-1948823.1	41	8	49	6	64	8
AD-1948824.1	33	4	39	5	49	6
AD-1948825.1	38	4	49	4	76	8
AD-1948826.1	40	4	46	4	61	7
AD-1948827.1	87	11	102	7	115	10
AD-1948828.1	33	6	43	2	57	7
AD-1948829.1	44	6	51	4	71	12
AD-1948830.1	43	7	67	10	89	5
AD-1948831.1	44	7	55	7	82	4
AD-1948832.1	34	5	36	4	46	3
AD-1948833.1	46	6	47	4	59	6
AD-1948834.1	37	5	44	4	68	3
AD-1948835.1	41	7	46	10	60	3
AD-1948836.1	40	8	38	4	49	3
AD-1948837.1	51	10	60	4	79	16
AD-1948838.1	55	8	72	6	79	11
AD-1948839.1	45	5	51	1	61	11
AD-1948840.1	39	4	41	2	49	4
AD-1948841.1	42	5	48	9	61	8
AD-1948842.1	49	6	73	9	80	8
AD-1948843.1	82	3	64	2	60	9
AD-1948844.1	35	5	40	6	57	4
AD-1948845.1	64	8	76	5	97	5
AD-1948846.1	31	7	42	5	55	4

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948847.1	36	4	45	6	56	8
AD-1948848.1	28	4	35	3	46	3
AD-1948849.1	44	2	48	4	64	7
AD-1948850.1	36	6	43	3	54	6
AD-1948851.1	51	3	51	6	61	5
AD-1948852.1	38	5	45	4	58	8
AD-1948853.1	50	1	58	10	64	9
AD-1948854.1	23	4	34	3	52	9
AD-1948855.1	39	4	49	5	66	15
AD-1948856.1	28	3	39	2	46	8
AD-1948857.1	34	5	45	6	61	8
AD-1948858.1	46	8	56	4	74	9
AD-1948859.1	46	6	51	7	68	8
AD-1948860.1	52	9	68	5	86	4
AD-1948861.1	42	4	59	7	92	8
AD-1948862.1	34	7	41	4	55	8
AD-1948863.1	53	11	60	4	88	7
AD-1948864.1	27	6	36	5	56	11
AD-1948865.1	44	10	50	7	78	5
AD-1948866.1	84	16	55	4	66	6
AD-1948867.1	53	9	51	8	68	1
AD-1948868.1	40	5	45	4	64	8
AD-1948869.1	32	4	38	4	47	6
AD-1948870.1	39	4	37	9	52	9
AD-1948871.1	33	6	43	5	54	11
AD-1948872.1	43	4	53	5	84	4
AD-1948873.1	39	6	43	3	53	4
AD-1948874.1	49	10	49	2	62	5
AD-1948875.1	42	7	44	3	63	10
AD-1948876.1	44	4	57	6	88	11
AD-1948877.1	32	5	40	6	63	6
AD-1948878.1	38	6	48	5	77	10
AD-1948879.1	29	5	36	3	51	7
AD-1948880.1	44	6	44	4	58	7
AD-1948881.1	30	5	38	3	48	6
AD-1948882.1	38	5	47	7	76	6
AD-1948883.1	38	9	51	8	58	5
AD-1948884.1	32	3	43	5	50	11
AD-1948885.1	43	6	48	6	58	10
AD-1948886.1	29	4	37	3	45	7

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948887.1	48	4	59	8	80	8
AD-1948888.1	34	5	42	5	53	13
AD-1948889.1	49	7	51	9	64	9
AD-1948890.1	37	4	39	6	59	9
AD-1948891.1	49	5	53	7	70	8
AD-1948892.1	36	6	46	4	70	13
AD-1948893.1	43	8	53	6	71	11
AD-1948894.1	45	8	65	3	94	10
AD-1948895.1	49	9	51	8	81	8
AD-1948896.1	42	8	50	4	71	7
AD-1948897.1	42	7	51	5	59	9
AD-1948898.1	37	9	46	3	62	7
AD-1948899.1	34	8	52	3	72	9
AD-1948900.1	37	3	61	11	84	10
AD-1948901.1	34	8	64	8	91	4
AD-1948902.1	31	6	65	6	74	12
AD-1948903.1	45	7	69	7	97	6
AD-1948904.1	25	7	35	3	58	11
AD-1948905.1	35	6	45	5	68	9
AD-1948906.1	25	6	38	5	59	6
AD-1948907.1	37	7	49	5	73	10
AD-1948908.1	37	7	41	4	57	10
AD-1948909.1	42	5	55	8	79	7
AD-1948910.1	33	7	41	5	57	6
AD-1948911.1	33	11	46	8	75	7
AD-1948912.1	23	4	35	2	54	10
AD-1948913.1	31	7	40	5	68	7
AD-1948914.1	26	7	39	2	49	8
AD-1948915.1	38	7	46	8	67	10
AD-1948916.1	32	7	36	9	59	6
AD-1948917.1	31	3	47	9	81	22
AD-1948918.1	40	4	49	9	79	8
AD-1948919.1	26	4	43	8	63	8
AD-1948920.1	35	4	54	5	77	7
AD-1948921.1	41	5	47	5	73	13
AD-1948922.1	33	6	43	5	70	10
AD-1948923.1	39	5	51	9	80	9
AD-1948924.1	25	4	36	3	49	5
AD-1948925.1	37	7	49	8	66	10
AD-1948926.1	27	3	35	4	50	5

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948927.1	36	5	47	7	59	6
AD-1948928.1	25	4	36	3	50	7
AD-1948929.1	47	4	64	7	87	3
AD-1948930.1	35	7	48	4	73	5
AD-1948931.1	28	6	40	9	59	11
AD-1948932.1	23	4	36	7	55	7
AD-1948933.1	29	2	40	5	52	10
AD-1948934.1	25	3	37	5	47	3
AD-1948935.1	31	4	46	10	69	6
AD-1948936.1	21	3	37	4	57	6
AD-1948937.1	25	4	40	7	69	8
AD-1948938.1	27	5	32	2	48	5
AD-1948939.1	32	5	39	5	56	8
AD-1948940.1	26	6	37	3	53	7
AD-1948941.1	33	4	46	4	69	8
AD-1948942.1	23	5	34	5	50	4
AD-1948943.1	28	5	39	5	58	5
AD-1948944.1	26	6	33	4	42	8
AD-1948945.1	34	4	39	3	54	7
AD-1948946.1	30	7	35	4	55	7
AD-1948947.1	42	7	43	6	60	12
AD-1948948.1	28	6	29	4	47	10
AD-1948949.1	49	3	72	8	108	8
AD-1948950.1	27	4	33	7	54	9
AD-1948951.1	46	3	53	7	80	10
AD-1948952.1	34	4	37	3	57	4
AD-1948953.1	45	6	53	6	82	7
AD-1948954.1	45	6	59	6	73	7
AD-1948955.1	40	10	54	5	86	6
AD-1948956.1	33	5	41	4	66	7
AD-1948957.1	41	4	47	10	75	13
AD-1948958.1	27	2	36	4	48	3
AD-1948959.1	37	6	44	4	67	6
AD-1948960.1	24	7	34	4	55	6
AD-1948962.1	20	5	31	3	34	10
AD-1948963.1	63	6	70	7	93	2
AD-1948964.1	16	2	28	2	40	10
AD-1948965.1	16	4	31	5	53	10
AD-1948966.1	24	3	31	3	54	8
AD-1948967.1	66	9	83	6	96	7

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1948968.1	35	5	41	2	63	6
AD-1948969.1	33	4	36	4	53	7
AD-1948970.1	29	6	36	4	52	6
AD-1948971.1	21	5	32	3	48	8
AD-1948972.1	18	3	28	1	40	7
AD-1948973.1	27	2	37	5	59	5
AD-1948974.1	43	5	50	3	74	6
AD-1948975.1	36	9	46	9	50	8
AD-1948976.1	32	8	41	5	67	8
AD-1948977.1	33	6	45	7	55	8
AD-1948978.1	32	2	41	4	58	9
AD-1948979.1	34	7	44	8	55	10
AD-1948980.1	32	7	36	2	53	8
AD-1948981.1	45	7	54	4	71	10
AD-1948982.1	19	4	29	3	47	7
AD-1948983.1	38	6	53	7	67	9
AD-1948984.1	33	7	40	3	46	7
AD-1948985.1	55	4	60	2	73	10
AD-1948986.1	33	5	39	3	50	9
AD-1948987.1	47	7	50	8	62	11
AD-1948988.1	28	7	35	5	43	6
AD-1948989.1	47	7	52	8	66	9
AD-1948990.1	33	8	49	4	71	15
AD-1948991.1	34	8	44	7	65	11
AD-1948992.1	37	9	48	4	70	6
AD-1948993.1	46	11	50	4	62	13
AD-1948994.1	30	5	35	4	56	12
AD-1948995.1	31	4	40	3	64	10
AD-1948996.1	23	6	33	3	48	10
AD-1948997.1	36	6	41	7	64	14
AD-1948998.1	22	5	32	4	45	7
AD-1948999.1	28	4	42	7	54	7
AD-1949000.1	21	3	31	4	48	9
AD-1949001.1	28	8	35	4	51	8
AD-1949002.1	15	5	27	2	43	9
AD-1949003.1	31	8	41	3	58	7
AD-1949004.1	29	2	34	4	46	8
AD-1949005.1	44	7	50	5	71	8
AD-1949006.1	20	7	31	2	43	10
AD-1949007.1	33	2	44	7	67	7

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-1949008.1	25	5	34	6	34	5
AD-1949009.1	48	4	51	8	65	11
AD-1949010.1	26	6	34	2	53	13
AD-1949011.1	36	4	48	6	63	9
AD-1949012.1	23	4	33	3	39	5
AD-1949013.1	25	5	41	10	62	12
AD-1949014.1	21	5	30	4	38	8
AD-1949015.1	35	5	44	3	58	10
AD-1949016.1	20	7	28	4	43	10
AD-1949017.1	30	8	49	6	77	10
AD-1949018.1	22	4	34	5	53	8
AD-1949019.1	41	8	61	9	95	6
AD-1949020.1	19	4	30	5	45	11
AD-1949021.1	25	6	43	6	62	11
AD-1949022.1	21	6	34	4	42	9
AD-1949023.1	16	4	26	2	42	10
AD-1949024.1	17	4	24	4	44	9
AD-1949025.1	21	5	32	4	56	11
AD-1949026.1	20	5	28	3	49	11
AD-1949027.1	22	3	34	5	48	5
AD-1949028.1	14	3	22	4	39	12
AD-1949029.1	16	6	29	3	51	12
AD-1949030.1	15	6	26	4	43	9
AD-1949031.1	31	7	53	8	78	7
AD-1949032.1	31	12	35	4	47	7
AD-1949033.1	45	4	47	6	56	6
AD-1949034.1	21	7	29	3	41	9
AD-1949035.1	24	4	35	4	60	11
AD-1949036.1	11	2	25	4	36	9
AD-1949037.1	27	5	37	6	48	7
AD-1949038.1	17	6	28	4	47	12
AD-2017365.1	55	13	75	12	76	19
AD-2017366.1	64	17	73	6	72	3
AD-2017367.1	54	18	63	12	84	9
AD-2017368.1	84	11	73	15	90	14
AD-2017369.1	71	6	53	13	81	11
AD-2017370.1	75	9	78	17	81	18
AD-2017371.1	75	17	73	6	80	10
AD-2017372.1	61	9	71	9	78	13
AD-2017373.1	81	9	89	8	94	8

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017374.1	78	8	78	1	85	15
AD-2017375.1	57	6	83	5	81	4
AD-2017376.1	60	4	76	8	78	13
AD-2017377.1	61	9	75	11	88	11
AD-2017378.1	73	4	78	10	82	12
AD-2017379.1	70	7	87	15	96	12
AD-2017380.1	51	16	80	11	67	9
AD-2017381.1	79	21	86	6	71	8
AD-2017382.1	32	4	38	4	54	10
AD-2017383.1	38	3	44	13	67	12
AD-2017384.1	40	3	46	3	57	12
AD-2017385.1	38	3	47	4	63	16
AD-2017386.1	36	6	52	8	66	4
AD-2017387.1	45	6	59	8	65	5
AD-2017388.1	49	5	58	7	76	7
AD-2017389.1	42	4	49	8	60	2
AD-2017390.1	47	7	52	9	69	9
AD-2017391.1	44	7	49	9	66	5
AD-2017392.1	44	3	62	10	69	16
AD-2017393.1	50	8	60	12	74	8
AD-2017394.1	36	4	48	9	64	9
AD-2017395.1	46	5	63	10	85	7
AD-2017396.1	43	6	60	3	76	14
AD-2017397.1	48	5	57	7	89	10
AD-2017398.1	39	6	54	10	82	10
AD-2017399.1	51	5	70	9	90	6
AD-2017400.1	58	3	53	10	83	6
AD-2017401.1	46	4	54	8	77	10
AD-2017402.1	42	1	60	8	82	5
AD-2017403.1	49	3	63	6	89	7
AD-2017404.1	62	7	72	6	90	6
AD-2017405.1	76	9	84	9	93	10
AD-2017406.1	47	3	72	11	84	12
AD-2017407.1	55	6	70	7	104	6
AD-2017408.1	51	6	54	8	76	3
AD-2017409.1	51	6	69	10	97	11
AD-2017410.1	53	7	74	11	100	17
AD-2017411.1	45	7	57	4	70	12
AD-2017412.1	55	6	65	12	84	6
AD-2017413.1	48	6	59	4	85	6

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017414.1	40	3	53	8	77	8
AD-2017415.1	61	5	65	9	88	6
AD-2017416.1	67	7	54	7	73	8
AD-2017417.1	46	1	53	11	76	7
AD-2017418.1	54	3	53	8	75	11
AD-2017419.1	53	6	60	7	70	2
AD-2017420.1	59	4	49	9	60	3
AD-2017421.1	88	7	73	5	73	7
AD-2017422.1	28	4	45	7	69	4
AD-2017423.1	46	2	56	9	84	13
AD-2017424.1	39	1	47	6	67	9
AD-2017425.1	47	3	64	7	82	6
AD-2017426.1	52	6	73	14	92	10
AD-2017427.1	45	7	61	8	84	13
AD-2017428.1	40	7	56	11	81	7
AD-2017429.1	36	3	48	6	62	14
AD-2017430.1	47	5	51	6	71	8
AD-2017431.1	44	6	47	7	79	7
AD-2017432.1	43	5	56	10	79	5
AD-2017433.1	60	8	65	5	84	11
AD-2017434.1	16	3	38	6	68	10
AD-2017435.1	32	3	56	6	86	5
AD-2017436.1	33	4	51	8	77	13
AD-2017437.1	33	2	52	13	65	6
AD-2017438.1	25	3	44	5	60	7
AD-2017439.1	26	5	43	9	66	11
AD-2017440.1	30	4	56	11	85	4
AD-2017441.1	21	4	42	0	68	2
AD-2017442.1	31	4	43	9	66	8
AD-2017443.1	25	2	37	8	55	2
AD-2017444.1	31	4	43	6	65	7
AD-2017445.1	38	4	44	4	69	14
AD-2017446.1	28	3	46	3	65	4
AD-2017447.1	28	7	50	4	74	8
AD-2017448.1	38	4	49	7	64	7
AD-2017449.1	46	4	52	3	80	2
AD-2017450.1	43	3	46	5	67	3
AD-2017451.1	29	3	45	3	67	6
AD-2017452.1	25	3	43	11	67	6
AD-2017453.1	29	4	50	9	73	10

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017454.1	31	4	53	7	90	10
AD-2017455.1	17	4	43	4	71	11
AD-2017456.1	24	4	47	10	64	6
AD-2017457.1	25	5	49	9	68	8
AD-2017458.1	37	2	50	8	75	7
AD-2017459.1	60	6	63	9	87	2
AD-2017460.1	50	5	56	8	83	8
AD-2017461.1	53	3	61	6	82	7
AD-2017462.1	45	4	47	8	85	2
AD-2017463.1	61	6	58	7	88	6
AD-2017464.1	34	2	51	10	73	2
AD-2017465.1	39	6	62	8	103	10
AD-2017466.1	29	4	47	5	72	3
AD-2017467.1	41	4	65	6	102	4
AD-2017468.1	55	6	91	13	92	10
AD-2017469.1	52	4	79	7	107	9
AD-2017470.1	45	4	54	7	73	8
AD-2017471.1	46	3	63	8	94	15
AD-2017472.1	22	3	37	4	58	5
AD-2017473.1	25	5	57	9	87	17
AD-2017474.1	27	5	44	7	80	5
AD-2017475.1	31	4	49	6	77	6
AD-2017476.1	31	4	42	3	70	9
AD-2017477.1	36	5	48	6	78	8
AD-2017478.1	25	2	44	9	59	6
AD-2017479.1	36	2	51	6	79	13
AD-2017480.1	37	4	42	4	71	10
AD-2017481.1	56	6	64	4	90	5
AD-2017482.1	36	4	51	2	69	2
AD-2017483.1	53	5	68	8	100	2
AD-2017484.1	55	4	52	5	79	8
AD-2017485.1	58	7	87	12	109	8
AD-2017486.1	36	1	50	5	72	4
AD-2017487.1	41	7	65	6	95	12
AD-2017488.1	32	3	48	11	71	11
AD-2017489.1	37	5	50	6	67	8
AD-2017490.1	38	8	58	7	77	6
AD-2017491.1	49	6	69	5	100	4
AD-2017492.1	38	3	50	4	78	6
AD-2017493.1	43	4	60	11	97	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017494.1	36	3	47	6	70	9
AD-2017495.1	49	3	69	5	102	9
AD-2017496.1	42	4	52	7	69	4
AD-2017497.1	51	6	64	6	91	5
AD-2017498.1	41	6	57	6	92	6
AD-2017499.1	54	8	83	13	119	10
AD-2017500.1	42	3	51	4	68	9
AD-2017501.1	54	3	74	16	110	9
AD-2017502.1	41	2	61	9	80	12
AD-2017503.1	46	3	59	10	91	15
AD-2017504.1	32	3	51	4	78	12
AD-2017505.1	33	2	59	5	98	6
AD-2017506.1	35	4	43	2	68	8
AD-2017507.1	42	6	48	9	71	2
AD-2017508.1	38	5	50	9	68	5
AD-2017509.1	45	2	56	3	83	9
AD-2017510.1	41	4	49	7	64	3
AD-2017511.1	42	3	60	8	79	8
AD-2017512.1	33	3	59	7	93	6
AD-2017513.1	50	2	60	8	96	5
AD-2017514.1	46	1	56	9	80	5
AD-2017515.1	54	6	86	17	108	6
AD-2017516.1	40	4	51	8	78	9
AD-2017517.1	40	4	56	7	84	9
AD-2017518.1	36	3	48	3	70	10
AD-2017519.1	39	6	69	6	118	30
AD-2017520.1	41	5	55	8	78	11
AD-2017521.1	62	8	94	3	123	7
AD-2017522.1	38	5	52	7	63	10
AD-2017523.1	46	2	64	10	88	12
AD-2017524.1	31	6	49	7	62	12
AD-2017525.1	40	5	56	5	84	5
AD-2017526.1	33	3	60	1	88	8
AD-2017527.1	49	3	71	7	103	3
AD-2017528.1	42	6	59	9	87	6
AD-2017529.1	52	2	74	11	112	8
AD-2017530.1	40	3	54	6	69	12
AD-2017531.1	50	6	76	10	107	3
AD-2017532.1	59	3	87	6	78	9
AD-2017533.1	60	8	78	9	112	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017534.1	56	4	72	6	103	4
AD-2017535.1	44	4	43	8	72	9
AD-2017536.1	38	3	43	13	58	14
AD-2017537.1	41	1	57	8	82	12
AD-2017538.1	33	2	51	5	71	5
AD-2017539.1	34	2	51	4	89	3
AD-2017540.1	35	3	44	6	72	11
AD-2017541.1	44	6	57	11	83	7
AD-2017542.1	38	3	46	6	72	7
AD-2017543.1	47	4	74	12	98	6
AD-2017544.1	32	2	41	3	63	4
AD-2017545.1	47	6	57	7	77	9
AD-2017546.1	49	3	55	2	72	6
AD-2017547.1	32	3	53	7	84	7
AD-2017548.1	30	2	44	9	66	5
AD-2017549.1	39	2	58	11	92	5
AD-2017550.1	34	5	52	4	80	10
AD-2017551.1	28	7	58	4	77	12
AD-2017552.1	33	11	46	2	66	9
AD-2017553.1	50	5	68	4	100	9
AD-2017554.1	35	8	47	3	61	1
AD-2017555.1	43	8	56	4	85	7
AD-2017556.1	38	3	47	3	68	11
AD-2017557.1	52	7	61	8	100	12
AD-2017558.1	45	3	56	5	85	8
AD-2017559.1	53	7	72	11	116	4
AD-2017560.1	38	3	51	7	89	6
AD-2017561.1	58	4	68	2	102	7
AD-2017562.1	39	2	53	8	76	2
AD-2017563.1	49	5	61	4	96	1
AD-2017564.1	45	4	51	5	73	5
AD-2017565.1	59	5	73	13	98	10
AD-2017566.1	54	13	57	3	66	12
AD-2017567.1	31	6	40	2	56	9
AD-2017568.1	36	6	46	6	50	13
AD-2017569.1	26	3	39	5	58	5
AD-2017570.1	25	2	49	3	75	7
AD-2017571.1	32	3	49	9	69	5
AD-2017572.1	42	5	49	3	59	7
AD-2017573.1	30	2	41	5	54	6

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017574.1	38	6	53	6	67	4
AD-2017575.1	39	2	47	6	65	4
AD-2017576.1	42	3	56	9	80	6
AD-2017577.1	34	3	47	7	63	2
AD-2017578.1	46	6	52	6	74	6
AD-2017579.1	31	3	47	3	66	4
AD-2017580.1	34	5	56	13	89	13
AD-2017581.1	41	6	59	10	85	15
AD-2017582.1	33	5	55	3	81	15
AD-2017583.1	58	7	60	9	80	6
AD-2017584.1	38	1	44	3	62	6
AD-2017585.1	47	4	56	9	85	11
AD-2017586.1	44	4	49	8	64	7
AD-2017587.1	46	3	59	9	84	8
AD-2017588.1	30	5	47	8	64	2
AD-2017589.1	29	5	52	10	84	11
AD-2017590.1	38	3	56	8	76	6
AD-2017591.1	35	3	55	9	70	5
AD-2017592.1	45	5	63	8	88	6
AD-2017593.1	57	4	72	6	121	9
AD-2017594.1	46	6	53	6	79	6
AD-2017595.1	54	7	70	16	96	5
AD-2017596.1	52	4	53	4	76	6
AD-2017597.1	50	7	58	8	82	9
AD-2017598.1	31	4	44	7	65	7
AD-2017599.1	29	1	32	13	78	5
AD-2017600.1	27	4	37	5	61	4
AD-2017601.1	43	5	57	7	76	4
AD-2017602.1	32	3	38	5	63	8
AD-2017603.1	29	4	44	6	72	8
AD-2017604.1	24	3	39	5	55	7
AD-2017605.1	36	4	53	5	78	8
AD-2017606.1	25	4	47	5	66	5
AD-2017607.1	34	4	53	4	71	6
AD-2017608.1	32	2	44	6	62	8
AD-2017609.1	38	3	52	7	74	9
AD-2017610.1	47	2	45	4	55	5
AD-2017611.1	42	3	51	3	76	12
AD-2017612.1	32	2	41	6	57	5
AD-2017613.1	51	6	56	4	64	6

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017614.1	33	3	47	7	61	11
AD-2017615.1	43	5	60	6	88	6
AD-2017616.1	64	4	70	5	72	7
AD-2017617.1	84	3	98	7	113	6
AD-2017618.1	72	5	90	8	88	10
AD-2017619.1	56	4	106	11	117	8
AD-2017620.1	53	3	82	6	89	8
AD-2017621.1	81	3	129	11	128	10
AD-2017622.1	73	5	92	7	101	9
AD-2017623.1	97	15	125	7	133	3
AD-2017624.1	102	11	98	4	87	16
AD-2017625.1	118	8	124	14	117	9
AD-2017626.1	80	8	78	6	85	7
AD-2017627.1	105	6	122	3	110	7
AD-2017628.1	91	6	110	11	115	15
AD-2017629.1	87	9	113	21	84	10
AD-2017630.1	66	6	95	12	85	13
AD-2017631.1	114	14	104	6	104	10
AD-2017632.1	65	6	79	3	88	6
AD-2017633.1	101	2	108	4	111	5
AD-2017634.1	71	9	90	9	83	5
AD-2017635.1	102	3	121	10	112	6
AD-2017636.1	86	3	93	5	91	2
AD-2017637.1	98	10	119	6	116	7
AD-2017638.1	81	8	95	11	97	4
AD-2017639.1	98	13	112	5	114	6
AD-2017640.1	90	1	102	5	98	3
AD-2017641.1	89	5	114	7	113	11
AD-2017642.1	62	3	84	4	82	7
AD-2017643.1	101	5	102	5	109	18
AD-2017644.1	69	7	98	12	94	6
AD-2017645.1	86	8	111	16	87	5
AD-2017646.1	82	7	105	9	86	5
AD-2017647.1	140	15	111	12	116	10
AD-2017648.1	59	2	80	12	83	7
AD-2017649.1	91	2	117	14	114	6
AD-2017650.1	78	6	78	10	80	7
AD-2017651.1	122	11	122	7	129	7
AD-2017652.1	90	2	104	17	89	6
AD-2017653.1	102	9	101	17	122	11

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017654.1	52	2	81	5	84	8
AD-2017655.1	120	7	122	9	113	6
AD-2017656.1	79	10	80	12	79	8
AD-2017657.1	113	6	102	15	112	2
AD-2017658.1	76	4	88	18	93	10
AD-2017659.1	93	9	111	13	98	15
AD-2017660.1	71	6	81	10	74	10
AD-2017661.1	87	2	106	12	95	17
AD-2017662.1	68	5	80	5	73	6
AD-2017663.1	87	11	111	9	103	16
AD-2017664.1	62	11	83	3	82	2
AD-2017665.1	88	6	99	6	105	8
AD-2017666.1	86	3	89	10	86	6
AD-2017667.1	110	12	121	6	104	13
AD-2017669.1	85	6	114	6	106	9
AD-2017670.1	77	3	89	7	86	13
AD-2017671.1	81	7	111	11	103	11
AD-2017672.1	96	6	102	19	88	10
AD-2017673.1	68	9	98	8	104	19
AD-2017674.1	79	7	110	10	79	11
AD-2017675.1	84	8	109	16	112	14
AD-2017676.1	63	10	74	3	79	13
AD-2017677.1	114	10	122	17	122	7
AD-2017678.1	74	9	83	4	79	5
AD-2017679.1	127	14	122	14	128	4
AD-2017680.1	73	9	72	12	71	10
AD-2017681.1	123	12	134	15	132	7
AD-2017682.1	114	7	100	5	96	6
AD-2017683.1	142	5	140	5	125	15
AD-2017684.1	88	11	87	4	83	3
AD-2017685.1	105	9	128	9	110	10
AD-2017686.1	65	12	85	10	81	6
AD-2017687.1	126	5	132	21	122	4
AD-2017688.1	107	8	121	14	103	8
AD-2017689.1	108	10	121	23	113	25
AD-2017690.1	87	12	81	15	79	12
AD-2017691.1	126	16	110	12	106	4
AD-2017692.1	83	14	81	8	80	5
AD-2017693.1	87	14	100	9	103	10
AD-2017694.1	50	4	73	7	78	4

	10nM		1nM		0.1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2017695.1	87	6	102	4	108	8
AD-2017696.1	49	3	62	24	77	2
AD-2017697.1	61	13	103	13	107	11
AD-2017698.1	107	10	99	7	89	3
AD-2017699.1	87	6	109	14	100	19
AD-2017700.1	73	4	82	7	82	4
AD-2017701.1	102	12	112	26	104	5
AD-2017702.1	106	12	92	5	80	6
AD-2017703.1	113	16	121	4	106	13
AD-2017704.1	101	3	96	9	97	14
AD-2017705.1	118	9	126	24	86	17
AD-2017706.1	89	11	76	4	74	13
AD-2017707.1	103	7	131	9	107	28
AD-2017708.1	60	10	81	13	63	10
AD-2017709.1	80	11	113	19	103	12
AD-2017710.1	47	8	73	5	73	8
AD-2017711.1	71	3	123	11	126	19
AD-2017712.1	83	5	80	17	68	4
AD-2017713.1	72	4	110	17	116	10
AD-2017714.1	41	6	80	8	78	13
AD-2017715.1	75	7	100	28	106	16
AD-2017716.1	85	6	86	10	79	5
AD-2017717.1	67	4	124	17	112	14
AD-2017718.1	56	10	77	2	77	15
AD-2017719.1	98	3	116	13	119	10
AD-2017722.1	68	7	88	15	80	14
AD-2017723.1	75	11	81	22	86	10
AD-2017725.1	84	11	94	14	87	17
AD-2017726.1	67	7	74	11	68	14
AD-2017727.1	81	10	89	11	109	3
AD-2017728.1	73	12	84	9	70	1
AD-2017730.1	77	9	92	15	86	5
AD-2017731.1	98	10	105	18	111	10
AD-2017732.1	91	5	92	9	83	12
AD-2017733.1	102	16	124	20	111	12
AD-2017734.1	50	5	83	8	69	13

Table 9. Multi-Dose *In vitro* Screen Free-Uptake of GRB14 dsRNA Agents in PCH Cells

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123156.1	55	8	61	6	72	8	92	5
AD-2123157.1	59	2	79	31	106	46	99	43
AD-2123159.1	52	3	45	8	61	3	79	6
AD-2123158.1	61	12	47	3	57	8	90	27
AD-2123161.1	51	5	47	5	60	8	75	7
AD-2123160.1	58	30	42	6	54	4	68	7
AD-2123162.1	45	3	48	7	49	5	69	9
AD-2123163.1	55	7	57	10	71	21	83	9
AD-2123165.1	43	2	39	4	48	4	71	8
AD-2123164.1	53	1	52	2	62	3	80	4
AD-2123166.1	50	3	50	3	58	4	70	7
AD-2123167.1	57	3	54	5	81	28	79	6
AD-2123170.1	51	3	47	7	61	5	77	3
AD-2123169.1	58	5	56	4	58	7	82	4
AD-2123168.1	70	6	62	7	68	7	83	1
AD-2123173.1	39	6	34	5	41	8	65	8
AD-2123171.1	51	2	46	5	56	6	74	3
AD-2123172.1	54	8	52	4	62	10	82	13
AD-2123175.1	43	4	46	3	48	5	82	15
AD-2123176.1	48	3	40	5	56	8	78	5
AD-2123174.1	52	4	49	8	54	6	74	5
AD-2123138.1	39	6	33	5	58	10	63	4
AD-2123137.1	49	7	43	8	59	6	69	4
AD-2123140.1	45	3	37	4	55	5	67	5
AD-2123139.1	45	6	38	5	53	5	72	2
AD-2123142.1	29	5	33	4	46	6	61	5
AD-2123141.1	42	5	39	6	59	4	67	8
AD-2123143.1	56	6	55	6	78	6	89	6
AD-2123177.1	57	7	56	6	62	4	87	11
AD-2123178.1	61	7	64	20	70	9	79	3
AD-2123179.1	97	15	94	5	93	9	103	6
AD-2123182.1	44	4	48	3	59	4	76	13
AD-2123180.1	54	9	44	3	55	5	71	4
AD-2123181.1	62	3	58	7	64	5	78	2
AD-2123183.1	42	5	37	6	48	3	79	21
AD-2123185.1	44	7	47	8	47	5	78	10
AD-2123184.1	52	4	44	4	60	4	78	7
AD-2123186.1	49	9	43	3	55	6	72	3
AD-2123188.1	50	9	48	2	55	3	76	5

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123187.1	53	3	51	8	60	4	85	12
AD-2123190.1	67	6	67	5	78	8	87	6
AD-2123191.1	72	5	58	8	72	9	80	3
AD-2123189.1	74	3	74	6	74	2	89	3
AD-2123192.1	54	4	51	5	55	2	74	2
AD-2123194.1	56	5	62	9	63	4	91	9
AD-2123193.1	64	5	72	6	66	5	98	19
AD-2123195.1	56	9	53	9	68	7	76	8
AD-2123196.1	77	6	72	7	80	5	99	11
AD-2123197.1	87	13	91	17	76	15	94	10
AD-2123198.1	80	8	79	15	72	8	86	9
AD-2123199.1	84	4	86	17	76	12	90	5
AD-2123200.1	76	14	75	11	69	10	81	4
AD-2123201.1	78	8	116	26	83	10	91	6
AD-2123203.1	63	5	66	10	63	11	86	6
AD-2123202.1	66	9	67	5	70	17	84	6
AD-2123205.1	52	9	55	5	50	6	73	5
AD-2123206.1	58	5	53	7	60	3	73	5
AD-2123204.1	60	6	73	12	61	5	81	4
AD-2123208.1	64	2	71	15	60	2	81	8
AD-2123207.1	67	4	65	4	61	5	76	4
AD-2123209.1	83	9	86	12	104	26	96	12
AD-2123210.1	45	4	52	11	55	2	77	7
AD-2123211.1	48	2	51	8	58	4	76	5
AD-2123212.1	53	3	58	11	69	9	103	27
AD-2123215.1	39	2	38	2	42	9	66	3
AD-2123214.1	41	4	42	8	50	6	61	2
AD-2123213.1	45	5	38	5	50	4	67	2
AD-2123218.1	56	6	55	7	61	7	83	7
AD-2123216.1	65	4	58	7	68	3	76	8
AD-2123217.1	68	7	64	7	74	5	81	3
AD-2123219.1	58	6	64	3	70	6	88	6
AD-2123220.1	61	6	54	6	60	5	76	11
AD-2123222.1	56	5	53	7	57	7	81	8
AD-2123221.1	70	8	65	5	77	17	89	5
AD-2123224.1	61	5	68	9	81	4	89	9
AD-2123223.1	62	7	54	3	61	2	73	6
AD-2123226.1	56	3	54	6	61	5	82	10
AD-2123225.1	63	7	64	7	80	19	79	8
AD-2123229.1	54	3	44	4	54	6	69	1

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123228.1	54	7	54	7	57	9	79	6
AD-2123227.1	60	4	56	12	66	8	86	9
AD-2123230.1	43	2	33	3	48	2	66	4
AD-2123231.1	44	8	41	4	51	5	75	10
AD-2123232.1	55	11	47	7	65	9	77	11
AD-2123234.1	53	7	55	4	63	8	81	8
AD-2123233.1	58	6	56	3	71	10	87	8
AD-2123236.1	82	7	73	6	85	16	100	7
AD-2123235.1	84	3	78	9	84	6	94	10
AD-2123237.1	39	3	35	1	46	5	62	7
AD-2123238.1	50	5	46	11	53	3	72	7
AD-2123239.1	81	16	61	14	70	13	96	19
AD-2123241.1	70	12	68	3	70	10	85	15
AD-2123240.1	81	15	79	5	75	8	99	16
AD-2123244.1	61	8	60	12	79	15	98	14
AD-2123242.1	72	14	65	7	85	13	103	10
AD-2123243.1	95	7	80	10	95	8	112	9
AD-2122978.1	49	7	43	2	71	8	67	6
AD-2122976.1	55	12	41	4	56	6	83	19
AD-2122977.1	58	3	61	8	67	7	87	2
AD-2122980.1	61	3	61	3	84	6	88	12
AD-2122979.1	65	4	70	5	78	8	87	1
AD-2122983.1	50	5	58	8	72	3	87	13
AD-2122981.1	52	3	56	4	65	4	79	12
AD-2122982.1	55	7	69	15	68	5	84	10
AD-2122985.1	53	3	52	4	70	6	81	7
AD-2122984.1	56	4	52	5	77	7	84	8
AD-2122987.1	65	4	61	4	73	17	82	13
AD-2122986.1	69	3	64	3	75	8	89	5
AD-2122989.1	37	3	36	2	50	5	67	10
AD-2122988.1	40	3	36	4	43	3	68	1
AD-2122990.1	36	2	32	7	47	4	65	3
AD-2122991.1	39	3	48	6	50	4	65	12
AD-2122992.1	41	3	56	10	64	5	82	11
AD-2122993.1	45	3	38	3	58	7	69	6
AD-2122995.1	59	7	55	5	77	7	74	7
AD-2122994.1	64	11	60	9	72	8	85	13
AD-2122996.1	58	2	55	6	66	6	90	8
AD-2122998.1	59	3	65	5	77	3	99	8
AD-2122997.1	70	3	62	5	75	5	81	4

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123000.1	65	10	69	4	88	8	89	6
AD-2122999.1	76	5	76	9	90	4	93	7
AD-2123001.1	85	8	90	14	95	9	101	4
AD-2123004.1	37	4	40	2	53	6	62	2
AD-2123002.1	38	3	39	5	51	3	66	11
AD-2123003.1	43	5	39	4	53	7	67	1
AD-2123005.1	36	3	36	4	47	4	67	8
AD-2123006.1	48	7	45	4	66	6	83	4
AD-2123007.1	55	4	52	4	69	3	87	4
AD-2123009.1	48	5	44	3	64	3	80	3
AD-2123008.1	53	5	55	5	58	6	83	2
AD-2123010.1	36	6	37	2	48	3	63	4
AD-2123011.1	42	4	43	2	49	5	70	5
AD-2123012.1	60	4	61	9	76	5	85	9
AD-2123013.1	63	8	67	3	69	8	87	7
AD-2123014.1	47	6	50	6	65	9	90	9
AD-2123016.1	35	2	36	2	40	4	59	5
AD-2123017.1	39	5	40	5	47	4	66	2
AD-2123019.1	44	4	47	3	59	3	75	7
AD-2123018.1	54	7	50	8	61	5	81	10
AD-2123020.1	34	2	37	3	45	5	67	3
AD-2123021.1	35	1	35	2	58	8	96	16
AD-2123022.1	35	6	35	4	42	6	59	8
AD-2123024.1	36	3	40	4	50	7	66	3
AD-2123023.1	43	2	42	3	55	7	74	8
AD-2123025.1	47	4	47	3	55	9	73	5
AD-2123026.1	50	8	51	3	60	5	79	7
AD-2123027.1	40	4	37	5	50	4	67	3
AD-2123028.1	44	4	59	12	53	7	63	7
AD-2123030.1	69	7	55	8	79	4	83	10
AD-2123029.1	85	8	82	12	87	8	100	8
AD-2123031.1	44	5	40	5	42	5	68	5
AD-2123032.1	48	6	47	6	57	7	72	2
AD-2123144.1	60	5	57	9	85	5	94	16
AD-2123145.1	63	10	58	9	77	15	96	10
AD-2123146.1	80	3	70	8	90	7	93	12
AD-2123147.1	49	6	47	3	62	10	78	9
AD-2123148.1	51	6	47	3	68	4	91	16
AD-2123149.1	70	9	61	5	90	11	98	12
AD-2123034.1	46	7	54	9	58	5	69	8

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123033.1	61	10	83	25	70	9	80	2
AD-2123036.1	48	3	47	5	54	1	72	4
AD-2123035.1	56	5	49	3	57	10	72	10
AD-2123038.1	44	7	44	2	60	6	69	7
AD-2123037.1	57	12	43	6	55	9	73	8
AD-2123039.1	50	6	46	4	60	7	73	3
AD-2123040.1	54	4	49	6	56	3	72	9
AD-2123041.1	59	6	54	8	61	7	67	9
AD-2123042.1	62	10	50	9	60	10	65	10
AD-2123043.1	71	6	60	4	63	2	78	9
AD-2123044.1	92	13	69	7	111	20	92	9
AD-2123045.1	46	8	45	6	66	10	77	12
AD-2123046.1	68	8	58	5	71	7	81	5
AD-2123047.1	68	9	62	3	72	7	74	2
AD-2123048.1	37	6	34	4	49	4	66	6
AD-2123050.1	39	5	41	2	50	3	60	4
AD-2123049.1	39	4	36	7	47	2	59	8
AD-2123052.1	51	9	49	9	62	9	79	12
AD-2123051.1	71	12	72	17	83	8	80	8
AD-2123054.1	40	4	44	5	48	11	64	2
AD-2123053.1	47	3	46	5	54	4	72	3
AD-2123056.1	54	4	55	5	59	4	78	7
AD-2123055.1	56	5	51	7	54	7	82	9
AD-2123057.1	62	3	54	4	72	5	80	5
AD-2123058.1	68	10	58	3	74	4	88	13
AD-2123059.1	71	10	64	5	86	3	88	12
AD-2123060.1	74	28	59	6	78	6	84	16
AD-2123062.1	61	7	56	7	78	13	84	9
AD-2123063.1	74	7	70	11	87	15	96	23
AD-2123061.1	75	6	72	6	83	5	77	4
AD-2123065.1	65	12	58	4	75	10	78	11
AD-2123064.1	80	14	72	16	110	37	88	11
AD-2123067.1	76	4	93	28	101	0	180	151
AD-2123066.1	77	10	90	12	111	13	172	42
AD-2123068.1	93	24	77	3	93	12	100	17
AD-2123069.1	76	3	78	7	91	5	101	7
AD-2123070.1	81	7	76	4	86	8	113	23
AD-2123071.1	35	3	33	4	47	6	66	4
AD-2123072.1	37	6	54	28	56	4	84	21
AD-2123074.1	52	6	54	4	77	6	82	9

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123073.1	56	5	54	11	72	5	87	7
AD-2123150.1	57	9	60	7	79	12	86	15
AD-2123152.1	59	8	55	7	74	8	83	9
AD-2123151.1	75	13	67	1	83	10	91	9
AD-2123075.1	59	5	49	5	71	8	92	21
AD-2123076.1	69	6	58	8	78	9	77	13
AD-2123077.1	49	6	43	0	64	3	74	3
AD-2123079.1	52	3	52	3	72	5	78	9
AD-2123078.1	61	8	57	12	72	5	79	2
AD-2123081.1	40	2	40	4	50	2	76	12
AD-2123080.1	42	3	39	2	53	1	59	1
AD-2123082.1	44	2	46	4	55	2	64	11
AD-2123083.1	47	7	39	6	57	3	71	8
AD-2123153.1	47	4	44	4	66	7	84	13
AD-2123154.1	68	10	72	21	72	10	95	11
AD-2123155.1	69	11	69	4	87	9	85	8
AD-2123084.1	39	2	36	4	49	4	62	8
AD-2123086.1	39	2	40	2	57	2	68	3
AD-2123085.1	46	4	41	3	65	7	72	4
AD-2123087.1	37	3	34	4	44	2	61	6
AD-2123088.1	41	2	61	31	51	4	63	7
AD-2123090.1	53	8	51	5	68	3	79	7
AD-2123089.1	86	30	53	5	61	3	72	10
AD-2123091.1	51	3	45	6	63	5	78	9
AD-2123092.1	66	18	47	6	66	5	82	13
AD-2123094.1	45	4	40	5	60	7	71	5
AD-2123093.1	46	7	40	1	52	3	73	9
AD-2123095.1	82	29	54	6	56	3	106	70
AD-2123097.1	56	4	48	4	60	5	77	13
AD-2123098.1	61	6	63	12	75	4	81	7
AD-2123096.1	75	6	63	19	74	5	88	7
AD-2123099.1	51	3	50	4	66	4	70	3
AD-2123100.1	52	1	48	5	62	2	74	3
AD-2123102.1	50	2	44	5	59	4	70	8
AD-2123101.1	56	4	43	5	57	6	75	7
AD-2123103.1	48	1	47	2	56	7	67	4
AD-2123104.1	49	2	46	3	60	3	78	7
AD-2123105.1	57	5	54	7	71	2	78	4
AD-2123106.1	68	5	60	6	81	5	93	15
AD-2123108.1	49	3	42	7	59	2	73	6

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123107.1	58	7	57	6	77	4	80	8
AD-2123110.1	40	3	41	4	49	5	63	7
AD-2123109.1	46	4	38	2	53	3	64	8
AD-2123111.1	48	2	43	4	59	7	75	1
AD-2123112.1	38	2	40	4	49	5	63	4
AD-2123113.1	41	4	40	4	54	5	70	4
AD-2123114.1	45	4	43	6	56	6	76	3
AD-2123115.1	44	1	41	4	48	5	70	6
AD-2123117.1	46	6	43	5	52	4	66	7
AD-2123116.1	53	4	46	3	60	9	73	4
AD-2123118.1	42	5	42	5	54	3	65	6
AD-2123119.1	52	3	51	3	67	2	78	8
AD-2123120.1	32	3	31	2	43	5	59	12
AD-2123121.1	40	6	38	4	46	7	70	5
AD-2123124.1	40	4	39	1	48	4	67	9
AD-2123123.1	40	2	39	3	53	5	59	4
AD-2123122.1	54	7	47	4	62	4	83	11
AD-2123125.1	34	4	31	2	44	7	53	8
AD-2123126.1	45	4	41	3	54	1	63	3
AD-2123127.1	47	6	38	4	54	5	70	1
AD-2123128.1	39	3	33	3	48	6	66	13
AD-2123129.1	45	5	41	7	57	6	74	3
AD-2123130.1	48	3	43	5	54	8	70	6
AD-2123132.1	34	1	31	5	47	8	57	5
AD-2123131.1	38	1	38	4	52	6	66	6
AD-2123133.1	52	2	39	5	54	4	71	5
AD-2123134.1	33	8	34	5	51	5	70	6
AD-2123135.1	36	5	36	7	51	6	63	9
AD-2123136.1	38	4	38	2	51	6	62	8

Table 10. Multi-Dose *In vitro* Screen Free-Uptake of GRB14 dsRNA Agents in PHH Cells

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123156.1	25	2	26	4	33	2	45	9
AD-2123157.1	23	2	27	4	37	8	49	10
AD-2123159.1	29	4	33	6	34	6	56	4
AD-2123158.1	25	2	29	4	33	4	43	7
AD-2123161.1	28	5	30	4	29	1	45	10
AD-2123160.1	25	3	26	3	29	5	44	7

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123162.1	25	2	28	3	30	4	42	3
AD-2123163.1	33	3	35	2	31	3	44	3
AD-2123165.1	28	3	35	6	41	4	49	8
AD-2123164.1	22	3	26	5	38	4	57	1
AD-2123166.1	33	4	39	4	36	3	57	8
AD-2123167.1	42	3	44	3	55	2	79	14
AD-2123170.1	28	4	35	4	41	5	52	9
AD-2123169.1	37	4	39	3	45	8	68	8
AD-2123168.1	44	4	48	3	54	4	75	2
AD-2123173.1	25	6	26	3	30	2	48	7
AD-2123171.1	33	4	37	5	47	6	55	9
AD-2123172.1	32	2	36	7	38	4	61	8
AD-2123175.1	36	2	38	3	47	5	70	5
AD-2123176.1	40	5	36	4	55	1	71	3
AD-2123174.1	30	4	39	6	44	6	68	6
AD-2123138.1	27	6	26	3	38	6	51	8
AD-2123137.1	28	6	30	5	42	6	64	14
AD-2123140.1	29	3	30	4	41	1	54	9
AD-2123139.1	25	3	28	6	38	7	42	6
AD-2123142.1	19	4	22	5	29	4	44	15
AD-2123141.1	22	4	24	8	30	5	44	18
AD-2123143.1	21	3	25	4	36	4	55	19
AD-2123177.1	32	5	36	2	40	5	56	3
AD-2123178.1	31	2	36	7	36	3	55	3
AD-2123179.1	47	6	52	3	66	9	89	4
AD-2123182.1	36	2	36	2	46	5	72	8
AD-2123180.1	27	2	36	4	41	8	58	6
AD-2123181.1	39	3	49	3	58	8	75	3
AD-2123183.1	30	7	32	3	43	5	65	5
AD-2123185.1	28	6	32	5	45	7	51	6
AD-2123184.1	42	6	34	5	52	2	69	9
AD-2123186.1	27	5	26	4	31	4	42	8
AD-2123188.1	30	2	36	4	40	6	67	13
AD-2123187.1	31	5	35	2	37	2	57	8
AD-2123190.1	57	4	56	4	78	9	87	5
AD-2123191.1	59	5	61	6	71	6	94	4
AD-2123189.1	50	2	57	3	64	4	90	11
AD-2123192.1	41	3	41	6	50	6	70	13
AD-2123194.1	39	3	35	3	45	8	59	12
AD-2123193.1	48	6	53	4	70	3	75	5

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123195.1	40	5	36	3	49	6	71	4
AD-2123196.1	54	3	56	8	63	6	82	10
AD-2123197.1	54	3	50	3	67	5	90	8
AD-2123198.1	92	29	57	6	68	10	87	10
AD-2123199.1	69	7	70	7	86	13	88	11
AD-2123200.1	51	4	52	5	60	7	81	8
AD-2123201.1	43	6	45	7	49	7	94	20
AD-2123203.1	42	2	44	3	61	11	86	15
AD-2123202.1	38	6	35	8	56	2	79	16
AD-2123205.1	37	3	38	5	51	8	63	12
AD-2123206.1	48	6	44	6	60	11	82	14
AD-2123204.1	37	2	38	6	48	4	82	20
AD-2123208.1	35	4	40	3	63	11	75	7
AD-2123207.1	37	2	45	4	61	3	83	12
AD-2123209.1	54	6	54	5	59	6	83	4
AD-2123210.1	24	3	28	4	41	5	51	5
AD-2123211.1	31	4	33	4	42	7	52	3
AD-2123212.1	28	1	34	5	40	6	58	4
AD-2123215.1	26	5	28	4	37	2	44	8
AD-2123214.1	32	1	36	2	49	7	50	6
AD-2123213.1	29	4	31	6	42	5	55	4
AD-2123218.1	31	4	34	5	39	5	59	9
AD-2123216.1	40	6	43	7	55	6	58	4
AD-2123217.1	42	6	42	5	41	3	69	8
AD-2123219.1	38	3	41	4	50	13	66	9
AD-2123220.1	40	6	36	6	45	11	68	9
AD-2123222.1	31	5	34	5	50	12	57	9
AD-2123221.1	44	3	48	7	60	10	83	7
AD-2123224.1	37	7	40	8	40	3	55	3
AD-2123223.1	35	7	35	4	52	4	57	6
AD-2123226.1	34	5	34	7	45	8	59	11
AD-2123225.1	35	6	34	5	42	6	61	12
AD-2123229.1	37	4	29	5	37	5	46	4
AD-2123228.1	35	3	35	7	40	5	57	8
AD-2123227.1	38	6	39	6	48	4	71	12
AD-2123230.1	29	2	28	3	37	5	40	6
AD-2123231.1	31	6	31	5	27	4	41	8
AD-2123232.1	33	4	30	5	28	5	46	9
AD-2123234.1	28	3	36	4	39	11	54	7
AD-2123233.1	32	5	31	6	37	5	64	9

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123236.1	66	11	68	7	61	10	84	20
AD-2123235.1	61	8	66	14	82	9	86	10
AD-2123237.1	26	5	24	4	32	3	42	10
AD-2123238.1	35	3	32	1	45	5	55	4
AD-2123239.1	25	4	25	4	29	3	46	1
AD-2123241.1	36	5	31	5	40	4	56	8
AD-2123240.1	38	7	33	5	41	6	58	13
AD-2123244.1	39	7	36	8	51	3	66	9
AD-2123242.1	40	8	30	9	45	4	61	10
AD-2123243.1	44	5	56	11	74	11	71	10
AD-2122978.1	28	3	29	4	41	11	47	4
AD-2122976.1	30	3	36	5	39	4	47	4
AD-2122977.1	34	2	40	4	47	11	54	7
AD-2122980.1	38	4	46	7	62	14	74	9
AD-2122979.1	35	5	38	7	53	20	66	6
AD-2122983.1	32	3	38	7	45	9	71	11
AD-2122981.1	30	4	33	3	49	10	62	11
AD-2122982.1	28	1	42	7	47	5	69	6
AD-2122985.1	36	3	37	3	45	4	75	8
AD-2122984.1	33	3	32	6	47	2	78	11
AD-2122987.1	49	4	45	4	48	8	83	5
AD-2122986.1	43	3	42	6	56	7	74	7
AD-2122989.1	31	5	35	3	41	7	62	8
AD-2122988.1	33	5	38	3	36	3	60	5
AD-2122990.1	35	5	37	8	42	7	63	5
AD-2122991.1	27	3	38	6	42	8	64	9
AD-2122992.1	32	4	35	6	42	5	75	5
AD-2122993.1	31	2	33	7	40	9	67	5
AD-2122995.1	55	5	59	7	60	8	92	13
AD-2122994.1	49	12	45	9	60	7	93	6
AD-2122996.1	46	3	45	4	62	3	80	1
AD-2122998.1	47	5	52	4	67	6	87	6
AD-2122997.1	45	7	58	11	60	11	89	5
AD-2123000.1	51	6	48	7	59	7	83	15
AD-2122999.1	69	6	73	5	81	8	98	8
AD-2123001.1	82	13	87	9	93	7	100	8
AD-2123004.1	32	6	38	5	45	4	66	7
AD-2123002.1	37	5	41	3	49	7	63	1
AD-2123003.1	40	3	46	7	50	9	66	4
AD-2123005.1	33	5	38	4	44	9	60	7

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123006.1	35	5	39	4	42	3	51	8
AD-2123007.1	33	4	34	2	45	7	57	14
AD-2123009.1	33	3	44	2	54	4	66	9
AD-2123008.1	31	3	41	7	48	2	61	12
AD-2123010.1	32	4	40	2	49	5	67	3
AD-2123011.1	40	4	48	8	51	6	75	3
AD-2123012.1	48	5	49	7	68	6	81	7
AD-2123013.1	53	3	63	9	75	4	96	6
AD-2123014.1	27	3	34	3	38	6	63	5
AD-2123016.1	31	4	29	2	30	8	47	3
AD-2123017.1	26	2	29	5	31	9	49	4
AD-2123019.1	39	3	42	4	53	4	72	5
AD-2123018.1	40	6	39	7	54	3	82	4
AD-2123020.1	24	6	32	4	43	6	60	8
AD-2123021.1	31	4	29	4	31	4	54	3
AD-2123022.1	34	2	32	5	32	6	48	1
AD-2123024.1	35	4	41	4	40	3	59	5
AD-2123023.1	37	5	41	4	52	7	61	6
AD-2123025.1	38	3	40	3	45	3	70	6
AD-2123026.1	40	2	49	4	55	5	76	9
AD-2123027.1	32	3	33	4	43	4	62	5
AD-2123028.1	33	3	33	3	43	2	66	6
AD-2123030.1	47	6	48	9	61	5	77	7
AD-2123029.1	48	4	66	11	63	5	91	7
AD-2123031.1	32	5	33	4	32	3	50	2
AD-2123032.1	31	2	40	6	43	3	59	4
AD-2123144.1	36	6	34	6	48	9	48	9
AD-2123145.1	48	10	48	9	60	6	63	10
AD-2123146.1	43	9	49	8	70	4	73	15
AD-2123147.1	30	5	33	7	49	5	76	15
AD-2123148.1	39	3	39	9	56	3	54	7
AD-2123149.1	42	6	38	5	50	0	60	7
AD-2123034.1	37	5	42	8	48	4	57	7
AD-2123033.1	49	10	51	9	54	3	76	10
AD-2123036.1	33	3	37	6	41	5	59	8
AD-2123035.1	42	7	39	7	46	6	71	8
AD-2123038.1	34	3	34	7	45	2	56	9
AD-2123037.1	33	7	34	4	41	6	57	7
AD-2123039.1	34	4	33	3	43	5	55	6
AD-2123040.1	37	10	41	8	47	5	60	8

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123041.1	44	11	44	6	52	5	69	4
AD-2123042.1	40	9	37	10	50	3	63	15
AD-2123043.1	36	5	39	5	51	4	64	9
AD-2123044.1	42	8	41	7	58	6	73	4
AD-2123045.1	23	2	24	2	32	5	48	8
AD-2123046.1	37	5	36	3	45	5	61	11
AD-2123047.1	39	8	44	7	57	3	76	8
AD-2123048.1	30	5	35	4	39	4	57	9
AD-2123050.1	28	2	33	2	35	2	48	6
AD-2123049.1	29	2	32	4	39	5	47	6
AD-2123052.1	33	7	33	6	47	7	62	13
AD-2123051.1	45	9	40	5	51	8	69	7
AD-2123054.1	30	4	28	7	42	8	53	8
AD-2123053.1	27	6	28	3	35	7	48	3
AD-2123056.1	32	5	32	3	42	6	55	7
AD-2123055.1	32	7	33	6	44	8	58	11
AD-2123057.1	33	5	38	3	47	4	62	8
AD-2123058.1	42	5	46	6	56	2	64	6
AD-2123059.1	39	7	36	9	52	7	56	12
AD-2123060.1	31	4	31	6	44	9	53	13
AD-2123062.1	26	6	26	7	44	4	60	6
AD-2123063.1	43	11	46	7	49	10	66	12
AD-2123061.1	33	5	40	6	51	7	61	7
AD-2123065.1	35	9	38	6	49	13	59	6
AD-2123064.1	49	13	52	10	65	10	72	20
AD-2123067.1	43	3	40	9	49	6	37	2
AD-2123066.1	35	7	42	16	50	10	55	4
AD-2123068.1	36	8	30	1	55	13	74	1
AD-2123069.1	35	10	37	4	39	2	74	21
AD-2123070.1	42	8	42	9	54	6	73	13
AD-2123071.1	33	5	27	5	31	6	56	19
AD-2123072.1	31	5	28	6	33	4	43	14
AD-2123074.1	31	2	33	4	40	6	26	11
AD-2123073.1	39	3	32	4	46	7	63	18
AD-2123150.1	34	6	32	5	44	8	62	22
AD-2123152.1	35	5	35	5	43	5	47	3
AD-2123151.1	34	6	37	7	46	7	52	12
AD-2123075.1	49	7	42	7	56	8	68	9
AD-2123076.1	62	4	48	4	63	7	64	12
AD-2123077.1	40	6	39	5	54	6	74	18

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123079.1	41	6	44	3	47	7	64	27
AD-2123078.1	47	4	51	5	49	10	89	20
AD-2123081.1	39	4	39	4	43	6	79	5
AD-2123080.1	39	6	39	3	44	5	79	17
AD-2123082.1	42	5	41	5	35	6	112	26
AD-2123083.1	36	4	43	8	49	5	56	4
AD-2123153.1	32	5	35	8	44	5	62	13
AD-2123154.1	55	11	62	11	64	11	79	31
AD-2123155.1	44	6	48	12	65	11	57	8
AD-2123084.1	39	6	36	1	32	8	53	12
AD-2123086.1	37	4	37	4	38	6	61	21
AD-2123085.1	49	5	49	7	53	2	78	19
AD-2123087.1	37	2	39	6	38	5	46	11
AD-2123088.1	44	8	38	3	42	5	80	32
AD-2123090.1	43	2	44	2	44	6	74	18
AD-2123089.1	44	7	46	5	53	5	77	15
AD-2123091.1	45	1	46	5	54	5	55	20
AD-2123092.1	46	3	51	2	65	2	83	6
AD-2123094.1	44	5	48	4	55	7	70	21
AD-2123093.1	44	4	43	3	51	7	66	26
AD-2123095.1	50	3	48	7	59	8	65	12
AD-2123097.1	38	6	48	2	53	3	67	14
AD-2123098.1	53	6	50	9	59	5	79	14
AD-2123096.1	50	8	51	10	64	12	38	2
AD-2123099.1	49	5	46	3	56	4	68	18
AD-2123100.1	46	5	44	3	55	7	68	18
AD-2123102.1	47	4	49	1	54	4	81	8
AD-2123101.1	45	3	48	4	57	3	67	10
AD-2123103.1	47	8	45	5	53	2	57	6
AD-2123104.1	37	3	41	4	50	5	58	14
AD-2123105.1	44	6	52	5	72	4	92	27
AD-2123106.1	59	7	65	9	67	8	97	19
AD-2123108.1	49	6	43	1	49	7	71	27
AD-2123107.1	57	7	54	5	69	6	106	29
AD-2123110.1	43	5	40	5	53	4	50	8
AD-2123109.1	43	5	42	4	53	6	73	16
AD-2123111.1	33	6	35	3	44	4	73	22
AD-2123112.1	29	2	31	2	38	3	43	17
AD-2123113.1	34	4	34	4	42	2	57	9
AD-2123114.1	40	4	37	5	45	6	61	20

	250nM		100nM		10nM		1nM	
Duplex ID	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV	% mRNA Remaining	STDEV
AD-2123115.1	36	4	38	3	50	4	54	14
AD-2123117.1	44	5	42	6	53	5	78	23
AD-2123116.1	49	7	46	6	65	6	96	22
AD-2123118.1	37	7	35	3	45	5	82	21
AD-2123119.1	36	4	35	5	53	4	54	16
AD-2123120.1	23	5	26	6	36	4	41	11
AD-2123121.1	29	4	29	5	40	5	49	5
AD-2123124.1	30	5	30	4	40	3	61	3
AD-2123123.1	32	6	28	4	43	3	64	4
AD-2123122.1	35	3	36	5	49	4	68	6
AD-2123125.1	27	3	28	7	37	6	46	18
AD-2123126.1	32	3	32	2	44	4	52	7
AD-2123127.1	31	7	30	4	39	3	46	13
AD-2123128.1	27	3	25	5	33	4	41	12
AD-2123129.1	37	8	40	3	51	4	57	7
AD-2123130.1	37	3	34	4	47	7	68	11
AD-2123132.1	27	8	28	4	36	5	39	4
AD-2123131.1	33	5	38	3	47	5	75	18
AD-2123133.1	37	6	37	3	42	5	64	14
AD-2123134.1	25	3	24	6	32	5	37	5
AD-2123135.1	25	4	26	2	35	5	41	1
AD-2123136.1	28	4	30	5	39	4	37	9

Table 11. GRB14 dsRNA IC50 Analysis: Free Uptake Assay in PCH and PHH Cells

		PCH		PHH	
Duplex ID	Conc. (nM)	% Message Remaining	STDEV	% Message Remaining	STDEV
AD-2123022.2	250	31.4	3.05	28.37	6.99
	25	34.27	3.01	31.01	1.69
	2.5	47.84	3.58	41.95	7.91
	0.25	70.6	6.17	69.96	6.95
	0.025	83.27	5.5	79.1	8.09
	0.0025	87	21.38	103.17	11.05
	0.00025	96.52	16	75.02	7.71
	0.000025	93.89	14.35	93.89	10.73
	0.0000025	92.16	18.47	76.07	11.88
	0.00000025	92.44	9.24	105.38	16.45
AD-2217245.1	250	35.19	6.66	25.4	3.72
	25	36.45	2.69	31.72	1.75
	2.5	47.94	3.8	40.08	4.32
	0.25	67.09	3.95	62.24	15.59
	0.025	79.04	5.09	81.88	12.08

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.0025	84.95	12.79	88.34	8.47
	0.00025	84.83	11.04	85.52	8.51
	0.000025	84.65	10.5	84.08	12.9
	0.0000025	87.51	7.79	80.01	12.76
	0.00000025	87.25	11.32	81.84	12.56
AD-2123112.2	250	33.47	5.14	19.79	2.25
	25	38.23	3.52	30.25	4.13
	2.5	56.25	6.94	39.84	4.84
	0.25	71.54	2.86	79.61	4.77
	0.025	83.1	9.78	99.62	27.77
	0.0025	82.33	6.76	114.43	14.27
	0.00025	94.14	5.64	95.19	11.2
	0.000025	85.68	9.1	93.46	7.41
	0.0000025	104.39	27.8	87.78	17.97
	0.00000025	103.68	25.12	100.11	14.48
AD-2217246.1	250	41.78	2.92	28.13	5.35
	25	47.41	5.42	37.55	5.26
	2.5	67.9	6.88	99.15	12.2
	0.25	76.7	3.85	93.25	6.65
	0.025	79.49	5.84	79.76	31.68
	0.0025	93.59	9.64	106.84	5.45
	0.00025	120.05	21.59	123.55	72.51
	0.000025	90.5	6.18	94.09	3.04
	0.0000025	108.51	22.68	135.96	70.2
	0.00000025	124.73	12.29	99.53	14.52
AD-2123113.2	250	36.3	4.75	25.72	5.14
	25	34.53	4	29.85	7.2
	2.5	58.07	7.69	45.56	6.59
	0.25	73.27	5.23	77.82	6.76
	0.025	85.31	8.12	89.15	8.71
	0.0025	122.2	20.01	114.7	14.42
	0.00025	124.98	12.46	90.45	7.54
	0.000025	104.2	19.3	113.4	7.51
	0.0000025	104.53	20.19	87.47	2.26
	0.00000025	118.86	21.52	108.09	8.22
AD-2217247.1	250	37.61	3.88	28.2	3.72
	25	44.4	3.03	36.71	4.43
	2.5	57.34	6.35	56.36	6.11
	0.25	75.36	6.11	83.1	4.17
	0.025	86.41	10.69	123.15	27.47
	0.0025	94.16	6.01	106.82	11.45
	0.00025	98.58	29.92	127.2	36.84
	0.000025	100.54	25.97	108.05	23.43
	0.0000025	94.75	22.9	107.03	5.65
	0.00000025	107.41	24.15	98.85	5.61
AD-2123125.2	250	34.4	4.63	25.57	1.01

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	25	38.84	2.4	33.21	4.87
	2.5	57.21	2.32	52.79	2.96
	0.25	81.56	7.97	83.35	6.37
	0.025	88.43	4.81	95.76	3.91
	0.0025	91.82	7.42	112.52	14.7
	0.00025	89.59	2.49	103.62	10.02
	0.000025	91.06	7.84	109.12	6.47
	0.0000025	95.37	12.11	101.18	2.5
	0.00000025	89.17	13.94	108.22	7.24
AD-2217248.1	250	49.1	10.68	34.22	8.74
	25	51.05	10.75	39.06	5.55
	2.5	67.87	8.38	58.35	5.06
	0.25	89.54	3.06	89.61	11.73
	0.025	100.13	5.95	115.01	10.17
	0.0025	94.19	7.74	113.65	10.31
	0.00025	102.14	7.78	103.12	6.44
	0.000025	97.81	3.24	117.87	24.94
	0.0000025	102.05	9.07	91.9	6.96
	0.00000025	92.51	11.12	88.17	3.67
AD-2123131.2	250	36.47	2.32	26.72	4.47
	25	44.5	3.96	34.01	2.93
	2.5	59.34	3.57	49.19	2.62
	0.25	81.7	6.79	89.76	13.83
	0.025	86.65	8.76	86.3	10.3
	0.0025	101.66	13.27	106.66	3.7
	0.00025	94.47	9.78	99.31	9.5
	0.000025	89.62	5.38	98.36	11.96
	0.0000025	93.89	12.09	96.97	7.47
	0.00000025	91.17	17.86	92.39	7.42
AD-2217249.1	250	38.68	3.66	27.34	2.32
	25	48.57	4.92	43.35	2.47
	2.5	68.86	6.08	58.99	2.48
	0.25	83	3.8	100.63	5.53
	0.025	90.78	8.97	96.62	9.36
	0.0025	100.13	11.68	117.36	4.96
	0.00025	94.63	6.68	98.44	6.37
	0.000025	97.17	11.69	116	14.67
	0.0000025	93.91	8.53	107.4	3.19
	0.00000025	109.75	21.45	105.54	7.57
AD-2123132.2	250	31.57	2.67	40.89	24.99
	25	39.63	2.42	30.44	4.03
	2.5	63.53	6.44	50.29	26.3
	0.25	78.94	6.41	80.81	1.02
	0.025	92.46	8.36	75.39	12.51
	0.0025	103.19	7.25	110.52	6.44
	0.00025	107.96	7.97	52.94	

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.000025	103.54	9.98	110.35	25.14
	0.0000025	105.92	25.26	64.99	2.87
	0.00000025	100.37	8.84	98.66	12.22
AD-2217250.1	250	33.69	1.07	28.05	4.71
	25	43.6	5.87	33.39	3.23
	2.5	62.94	3.82	46.85	3.79
	0.25	86.67	9.04	79.34	8.41
	0.025	96.01	4.68	103.74	20.79
	0.0025	104.29	7.85	121.2	8.21
	0.00025	103.4	3.8	111.34	10.92
	0.000025	102.35	12.95	117.46	7.38
	0.0000025	98.74	0.79	101.21	9.77
	0.00000025	120.58	8.16	105.08	5.48
AD-2123134.4	250	33.15	2.1	27.78	1.74
	25	40.81	2.65	33.76	3.56
	2.5	61.63	6.69	49.19	4.2
	0.25	83.56	12.33	81.09	8.08
	0.025	101.57	9.98	107.99	13.34
	0.0025	94.73	10.69	115.78	12.52
	0.00025	103.08	4.99	113.69	15.87
	0.000025	96.93	9.08	117.3	8.47
	0.0000025	99.16	2.27	120.24	12.3
	0.00000025	96.19	8.26	111.53	10.7
AD-2217251.1	250	37.69	2.29	31.96	13.79
	25	43.57	3.54	41.81	2.58
	2.5	62.4	5.68	57.86	1.83
	0.25	81.8	8.15	97.95	9.76
	0.025	107.28	11.78	110.06	8.71
	0.0025	99.93	11.33	116.63	15.23
	0.00025	92.55	3.69	109.66	8.17
	0.000025	97.63	7.09	128.33	14.4
	0.0000025	89.44	7.8	107.6	8.11
	0.00000025	94.54	4.96	113.21	6.05
AD-2123135.2	250	40.88	4.04	27.98	3.18
	25	46.6	5.52	38.22	2.31
	2.5	68.7	15.41	52.69	5.07
	0.25	93.7	4.23	85.7	9.88
	0.025	96.27	11.39	113.21	22.31
	0.0025	115.14	23.05	122.33	8.99
	0.00025	115.1	23.96	106.98	16.22
	0.000025	101.39	19.59	106.01	8.97
	0.0000025	95.96	13.5	95.25	25.78
	0.00000025	95.51	18.92	111.38	19.9
AD-2217252.1	250	35.36	3.79	27.3	6.32
	25	46.97	5.76	35.13	2.6
	2.5	64.92	11.21	52.38	2.98

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.25	79.03	8.16	90.77	3.82
	0.025	88.99	7.3	108.8	12.02
	0.0025	108.81	10.37	111.98	13.33
	0.00025	100.68	16.01	100.82	10.98
	0.000025	93.74	24.39	107.19	10.29
	0.0000025	82.9	10.14	101.5	10.61
	0.00000025	94.55	13.88	104.69	16.85
AD-2123136.2	250	42.53	2.66	23.62	4.67
	25	54.36	10.16	38.64	1.11
	2.5	66.52	8.03	49.38	8.58
	0.25	80.57	6.32	88.65	6.98
	0.025	98.57	9.25	92.86	13.22
	0.0025	104.99	8.4	120.29	13.06
	0.00025	106.48	11.29	109.31	15.09
	0.000025	95.44	13.42	125.38	17
	0.0000025	91.39	7.06	122.25	36.29
	0.00000025	96.13	12.08	114.04	10.11
AD-2217253.1	250	46.8	3.28	49.11	21.11
	25	53.12	8.58	41.14	1.42
	2.5	71.67	3.01	56.64	39.09
	0.25	91.1	13.65	95.52	7.86
	0.025	105.46	9.84	106.52	59.71
	0.0025	123.47	26.69	109.16	11.86
	0.00025	117.65	23.13	98.75	26.58
	0.000025	102.44	3.03	111.4	8.24
	0.0000025	97.89	12.58	54.74	8.02
	0.00000025	96.08	17.64	119.15	18.2
AD-2123142.4	250	36.46	4.22	21.28	3.49
	25	47.43	8	30.18	2.63
	2.5	64.95	6.49	41.18	2.51
	0.25	92.93	17.51	84.89	3.27
	0.025	117.71	21.05	117.97	38.72
	0.0025	115.28	17.76	121.31	9.68
	0.00025	102.9	15.09	133.16	16.51
	0.000025	100.41	8.58	120.92	5.91
	0.0000025	97.07	6.87	105.19	7.45
	0.00000025	97.96	7.91	116	22.73
AD-2217254.1	250	31.85	4.42	26.46	4.87
	25	44.98	8.64	33.39	3.07
	2.5	65.73	15.12	50.12	1.68
	0.25	91.7	7.1	85.21	4.26
	0.025	106.91	12.53	121.22	7.89
	0.0025	108.3	11.04	119.73	10.6
	0.00025	89.7	13.07	142.73	23.34
	0.000025	94.5	8.25	116.19	9.41
	0.0000025	98.1	7.28	114.44	15.01

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.00000025	96.26	9.86	120.12	13.6
AD-2123143.2	250	52.85	3.96	29.25	3.52
	25	68.89	10.94	46.53	1.85
	2.5	91.63	10.12	64.12	6.96
	0.25	91.25	6.68	103.99	14.46
	0.025	97.6	7.37	100.67	13.21
	0.0025	110.03	11.88	124.92	4.49
	0.00025	99.4	13.35	108.59	21.34
	0.000025	88.05	7.95	135.73	3.79
	0.0000025	92.67	7.3	120.66	12.39
	0.00000025	91.19	12.42	122.17	9.78
AD-2217255.1	250	62.34	8.7	28.88	2.54
	25	75.45	9.33	40.62	4.43
	2.5	83.23	1.78	59.44	10.88
	0.25	94.7	15.62	100.19	8.86
	0.025	100.04	7.46	96.01	9.82
	0.0025	96.55	13	109.41	5.18
	0.00025	102.91	16.22	96.41	16.92
	0.000025	93.7	7.5	114.75	15.15
	0.0000025	100	13.7	102.22	4.51
	0.00000025	104.41	15.61	107.72	11.21
AD-2123054.2	250	40.05	2.65	33.58	5.05
	25	43.52	2.84	38.7	2.33
	2.5	57.99	7.38	56.06	3.08
	0.25	74.01	6.13	91.49	10.19
	0.025	90.64	7.05	89.32	4.07
	0.0025	107.45	21.35	99.84	10.29
	0.00025	91.31	7.56	91.73	5.49
	0.000025	90.38	16.86	96.09	12.72
	0.0000025	90.32	14.74	93.89	9.36
	0.00000025	79.44	15.31	101.34	3.54
AD-2217262.1	250	37.42	2.29	24.18	3.07
	25	47.86	4.23	44.19	4.45
	2.5	62.42	4.24	54.6	8.88
	0.25	81.23	5.66	89.97	4.62
	0.025	86.9	8.24	73.36	51.93
	0.0025	96.19	4.94	111.14	11.87
	0.00025	89.07	3.49	96.72	4.06
	0.000025	86.93	8.56	106.25	5.44
	0.0000025	87.46	7.46	78.14	12.33
	0.00000025	103.55	12.82	106.41	8.58
AD-2123157.2	250	31.85	5.74	40	20.67
	25	46.09	7.67	32.43	1.84
	2.5	51.12	7.98	61.72	29.19
	0.25	76.69	7.05	75.67	8.65
	0.025	93.26	5.43	117.66	57.94

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.0025	107.06	8.61	107.79	19.92
	0.00025	101.68	10.18	185.57	97.21
	0.000025	96.64	3.57	97.85	1.4
	0.0000025	102.7	13.21	156.04	78.85
	0.00000025	88.21	12.97	95.7	3.06
AD-2217257.1	250	33.38	4.43	28.1	3.81
	25	43.67	4.07	35.24	3.13
	2.5	61.93	6.69	48.43	3.54
	0.25	76.63	9.33	85.59	5.07
	0.025	99.78	9.07	204.08	52.2
	0.0025	99.41	8.5	107.29	10.43
	0.00025	96.73	5.93	99.01	6.36
	0.000025	106.59	15.38	106.03	4.49
	0.0000025	89.05	1.83	96.15	11.26
	0.00000025	94.57	5.71	103.71	11.58
AD-2123162.2	250	28.03	2.78	23.83	1.41
	25	34.37	1.84	35.9	1.61
	2.5	56.93	5.16	50.99	4.86
	0.25	71.92	6.42	81.21	3.92
	0.025	84.14	16.3	91.75	67.81
	0.0025	105.21	18.32	104.63	6.12
	0.00025	97.88	5.41	108.24	6.2
	0.000025	99.24	11.09	113.1	9.54
	0.0000025	101.65	8.35	104.56	4.12
	0.00000025	97.62	6.96	109.16	10.88
AD-2217258.1	250	37.53	5.6	24.25	5.07
	25	44.02	2.12	44.49	4.53
	2.5	59.44	3.65	59.95	2.24
	0.25	80.36	7.37	95.76	5.1
	0.025	97.92	9.18	106.4	4.55
	0.0025	101.13	4.73	111.12	5.1
	0.00025	99.24	8.73	99.96	14.84
	0.000025	85.72	10.59	111.66	3.57
	0.0000025	98.01	4.27	103.31	12.47
	0.00000025	92.98	8.93	117.79	8.24

Table 12. GRB14 dsRNA IC50 Analysis: Transfection of PCH and PHH Cells

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
AD-2123022.2	10	13.8	2.08	31.9	2.87
	1	19.15	3.86	32.86	2
	0.1	39.83	5.45	42.11	5.6
	0.01	56.46	13.02	65.4	10.99
	0.001	98.75	12.78	86.87	5.52

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.0001	121.75	16.3	115.26	28.12
	0.00001	129.67	19.23	107.47	12
	0.000001	113.88	8.21	105.54	23.76
	0.0000001	123.68	7.43	100.41	14.52
	0.00000001	125.99	22.38	90.79	16.07
AD-2217245.1	10	15.15	1.16	30.03	4.56
	1	21.38	1.98	29.51	2.6
	0.1	31.15	4.5	48.91	7.15
	0.01	55.39	6.22	61.16	3.82
	0.001	96.36	8.79	90.42	11.89
	0.0001	109.87	10.44	120.93	21.2
	0.00001	104.76	9.87	103.4	20.52
	0.000001	105.11	12.14	114.46	11.22
	0.0000001	97.79	7.85	102.53	13.29
	0.00000001	109.34	19.75	101.2	15.32
AD-2123112.2	10	13.8	1.64	23.87	2.98
	1	17.55	1.98	30.6	2.65
	0.1	33.66	3.87	42.88	1.94
	0.01	58.73	6.95	72.45	8.56
	0.001	99.3	11.86	95.84	4.96
	0.0001	109.19	6.81	121.55	23.94
	0.00001	109.8	7.68	114.64	17.12
	0.000001	98.06	9	108.05	16.95
	0.0000001	112.21	6.02	87.88	9.44
	0.00000001	113.92	4.61	103.22	19.29
AD-2217246.1	10	19.14	2.25	33.65	26.24
	1	28.8	3.37	40.51	6.62
	0.1	50.15	5.61	46.33	13.93
	0.01	85.16	2.08	99.79	6.41
	0.001	115.02	7.24	94.23	35.17
	0.0001	99.24	4.64	125.96	9.67
	0.00001	125.93	15.21	93.65	38.35
	0.000001	107.7	10.3	108.47	10.33
	0.0000001	115.93	9.26	102.07	93.75
	0.00000001	105.62	18.68	104.78	22.64
AD-2123113.2	10	11.44	2.31	26.77	5.4
	1	17.82	2.58	33.64	4.27
	0.1	34.39	6.28	45.43	5.13
	0.01	67.56	7.74	80.1	10.89
	0.001	102.88	8.53	108.21	17.49
	0.0001	113.08	13.32	133.33	30.36
	0.00001	109.94	6.73	109.51	16.24
	0.000001	107.52	7.22	117.18	10.15
	0.0000001	97.94	6.89	103.62	22.78
	0.00000001	108.8	9.84	114.48	35.96
AD-2217247.1	10	12.51	1.33	26.67	2.1

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	1	21.35	4.29	31.69	4.19
	0.1	36.59	4.28	48.89	4.85
	0.01	77.11	5.57	85.91	9.17
	0.001	101.27	14.52	104.09	12.37
	0.0001	116.65	16.11	113.09	17.67
	0.00001	106.62	2.68	111.43	9.39
	0.000001	113.29	16.98	111.78	17.42
	0.0000001	105.59	8.88	107.32	20.25
	0.00000001	109.45	13.45	100.25	32.45
AD-2123125.2	10	10.42	1.55	22.77	1.7
	1	21.95	7.24	30.19	3.92
	0.1	32.27	4.36	46.02	1.4
	0.01	66.58	6.9	84.63	7.8
	0.001	99.21	10.62	101.15	11.45
	0.0001	108.04	6.35	112.64	6.82
	0.00001	103.78	13.05	110.28	18.32
	0.000001	102.23	9.56	113.35	18.68
	0.0000001	103.51	15.7	101.85	17.82
	0.00000001	114.11	4.33	116.53	15.25
AD-2217248.1	10	20.75	8.82	24.5	2.95
	1	27.12	6.17	35.85	3.4
	0.1	47.28	8.18	49.07	3.55
	0.01	72.76	15.52	89.93	14.84
	0.001	102.32	25.27	90.15	12.59
	0.0001	96.34	10.18	106.12	12.76
	0.00001	98.93	12.56	94.15	15.14
	0.000001	113.11	25.87	105.72	14.54
	0.0000001	102.47	26.93	89.73	7.43
	0.00000001	100.6	21.64	99.58	17.06
AD-2123131.2	10	27.43	7.63	49.91	4.75
	1	23.48	4.77	43.13	6.35
	0.1	48.7	13.16	51.85	7.51
	0.01	69.01	14.86	85.51	13.42
	0.001	85.69	7.91	103.87	12.05
	0.0001	83.11	12.62	93.36	21.26
	0.00001	102.04	24.14	93.65	11.33
	0.000001	87.44	8.94	97.15	21.63
	0.0000001	90.13	13.27	86.42	11.44
	0.00000001	94.35	15.39	93.31	16.77
AD-2217249.1	10	24.26	6.42	48.19	7.09
	1	21.15	3.94	50.85	4.6
	0.1	38.71	2.84	59.55	6.87
	0.01	76.13	15.15	113.9	2.55
	0.001	94.11	5.97	100.98	20.73
	0.0001	97.13	6.65	110.67	15.77
	0.00001	97.79	14.83	101.17	15.57

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.000001	97.8	6.82	110.79	13.36
	0.0000001	104.09	6.99	95.77	11.27
	0.00000001	101.19	14.74	107.15	16.53
AD-2123132.2	10	13.2	1.04	29.56	5.61
	1	15.09	1.93	35.07	1.25
	0.1	31.22	4.36	91.49	42.55
	0.01	67.48	17.7	78.99	5.12
	0.001	82.4	6.08	77.73	25.55
	0.0001	104.36	16.36	115.97	19.86
	0.00001	112.54	19.62	178.45	7
	0.000001	100.35	15.62	106.45	7.27
	0.0000001	98.84	21.06		
	0.00000001	101.38	9.32	103.77	19.3
AD-2217250.1	10	11.72	1.32	30.31	0.94
	1	17.03	2.93	35.26	2.88
	0.1	31.56	5.49	48.54	4.58
	0.01	62.41	14.86	81.59	8.89
	0.001	88.11	16.31	99.78	11.51
	0.0001	96.67	11.71	122.55	12.44
	0.00001	96.57	14.48	103.59	4.13
	0.000001	91.72	13.78	122.1	16.83
	0.0000001	100.14	5.67	111.37	20.6
	0.00000001	105.36	7.06	110.7	12.27
AD-2123134.4	10	6.74	1.91	21.21	2.56
	1	14.77	3.41	31.5	1.33
	0.1	27.84	2.64	43.28	3.77
	0.01	50.8	7.73	76.32	11.78
	0.001	90.94	11.13	109.99	10.23
	0.0001	84.25	9.52	117.77	15.19
	0.00001	99.45	28.28	114.4	10.18
	0.000001	97.7	8.09	105.88	28.87
	0.0000001	100.73	9.55	115.68	17.5
	0.00000001	93.34	6.74	107.42	22.33
AD-2217251.1	10	8.64	1.34	20.96	2.15
	1	22.46	10.35	33.99	2.61
	0.1	33.37	4.48	49.17	1.92
	0.01	74.86	18.67	94.88	5.37
	0.001	85.63	3.6	114.23	6.82
	0.0001	88.39	7.93	131.83	11.12
	0.00001	94.28	15.84	117.34	8.88
	0.000001	97.02	10.49	115.29	22.57
	0.0000001	97.94	8.87	114.88	17.21
	0.00000001	101.04	6.3	126.58	19.21
AD-2123135.2	10	17.73	6.32	25.33	4.04
	1	20.25	2.75	29.9	5.2
	0.1	32.45	3.16	48.05	2.62

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.01	62.59	17.7	76.62	13.84
	0.001	92.23	26.22	103.43	7.42
	0.0001	96.84	9.13	109.59	13.54
	0.00001	94.09	22.25	95.71	7.48
	0.000001	88.9	9.56	98.04	7.24
	0.0000001	93.25	9.48	95.1	8.25
	0.00000001	93.98	13.16	98.05	21.05
AD-2217252.1	10	10.74	3.89	22.63	0.6
	1	19.38	1.05	24.23	1.31
	0.1	34.21	4.43	45.22	3.89
	0.01	56.58	5.15	70.62	4.75
	0.001	78.86	6.37	88.15	7.99
	0.0001	90	14.57	116.05	5.71
	0.00001	80.65	26.32	99.65	16.73
	0.000001	90.23	11.99	105.93	9.65
	0.0000001	104.56	13.08	99.8	21.8
	0.00000001	95.87	7.19	98.84	22.47
AD-2123136.2	10	20.18	6.65	32.08	1.67
	1	18.14	2.58	38.6	1.59
	0.1	33.91	6.62	48.57	4.39
	0.01	51.22	4.09	73.26	10.78
	0.001	83.67	4.57	101.32	2.97
	0.0001	96.9	7.51	126.68	9
	0.00001	100.03	13.5	106.24	9
	0.000001	93.13	9.79	115.18	23.4
	0.0000001	110.2	14.63	107.44	7.5
	0.00000001	99.8	21.88	119.02	12.16
AD-2217253.1	10	12.52	2.16	42.29	15.46
	1	20.95	1.04	33.59	5.03
	0.1	31.55	4.36	77.43	37.51
	0.01	53.21	7.34	85.39	7.01
	0.001	89.66	13.47	56.09	
	0.0001	99.52	17.56	123.23	9.05
	0.00001	101.13	11.54	118.67	24.83
	0.000001	93.81	11.85	120.13	5.67
	0.0000001	106.16	7.12	65.79	
	0.00000001	108.42	7.89	123.21	27.41
AD-2123142.4	10	13.15	1.23	23.02	3.14
	1	25.73	4.35	29.77	1.22
	0.1	33.34	3.59	59.67	24.52
	0.01	52.27	12.02	74.3	7.61
	0.001	86.64	7.62	108.71	6.69
	0.0001	99.23	9.74	119.08	9.36
	0.00001	91.57	16.6	103.92	15.38
	0.000001	101.08	8.94	122.26	10.54
	0.0000001	101.25	5.45	119.41	8.2

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.00000001	102.62	8.27	119.53	17.59
AD-2217254.1	10	13.48	2.7	23.06	1.51
	1	18.24	3.35	28.37	1.43
	0.1	32.23	5.78	49.43	3.45
	0.01	53.91	3.52	79.47	5.45
	0.001	87.98	4.59	126.62	14.3
	0.0001	96.59	12	130.36	13.8
	0.00001	98.69	9.27	122.59	16.96
	0.000001	95.05	11.6	128.63	8.47
	0.0000001	99.78	11.93	120.17	6.58
	0.00000001	96.83	11.23	119.66	9.01
AD-2123143.2	10	27.05	3.3	38.22	1.87
	1	29.06	2.29	44.69	7.38
	0.1	38.9	6.76	59.21	5.92
	0.01	71.48	8.31	86.91	4.94
	0.001	96.63	14.31	132.21	17.53
	0.0001	97.06	12.27	129.99	8.71
	0.00001	88.18	8.17	123.6	16.09
	0.000001	91.54	20.28	131.9	14.27
	0.0000001	92.03	7.85	119.26	18.38
	0.00000001	105.88	15.1	125.32	18.58
AD-2217255.1	10	26.62	8.93	29.45	2.77
	1	29.92	2.89	33.59	2.97
	0.1	53.55	6.36	45.55	4.73
	0.01	75.36	2.09	70.54	9.38
	0.001	116.95	17.24	73.92	15.68
	0.0001	93.06	10.99	84.58	10.89
	0.00001	101.25	14.2	76.42	7.35
	0.000001	93.76	11.05	81.84	6.97
	0.0000001	90.56	23.54	78.08	6.49
	0.00000001	100.81	1.4	92.17	19.38
AD-2123054.2	10	20.62	1.51	33.72	3.16
	1	20.27	4	36.76	3.36
	0.1	28.79	6.37	44.2	0.59
	0.01	54.68	2.46	70.72	5.86
	0.001	80.48	5.71	80.8	2.58
	0.0001	96.52	6.24	90.85	9.12
	0.00001	84.79	2.07	81.18	5.29
	0.000001	94.57	22.89	79.15	14.73
	0.0000001	92.31	18.08	79.65	16.66
	0.00000001	93.69	10.39	84.27	10.46
AD-2217262.1	10	14.91	0.29	34.69	6.02
	1	20	2.21	44.64	4
	0.1	31.61	1.9	45.6	3.17
	0.01	55.17	3.88	85.92	4.79
	0.001	81.21	7.98	95.29	4.25

		PCH		PHH	
Duplex ID	**Conc. (nM)**	**% Message Remaining**	**STDEV**	**% Message Remaining**	**STDEV**
	0.0001	87.55	13.71	109.03	17.79
	0.00001	101.81	5.93	102.15	5.04
	0.000001	86.65	4.93	99.56	8.31
	0.0000001	99.97	10.18	89.09	7.79
	0.00000001	93.91	12.93	104.99	4.19
AD-2123157.2	10	11.21	2.33	31.29	18.72
	1	14.78	1.08	31.1	2.38
	0.1	26.99	3.48	50.88	28.61
	0.01	40.12	4.76	61.13	6.19
	0.001	78.69	10.79	149.43	10.85
	0.0001	116.84	26.17	114.67	8.59
	0.00001	136.62	6.17	69.84	14.28
	0.000001	102.52	15.23	123.94	14.8
	0.0000001	107.71	18.21	50.9	7.95
	0.00000001	116.74	28.74	101.38	16.65
AD-2217257.1	10	10.74	2.98	22.17	2.52
	1	16.62	3.1	31.99	1.7
	0.1	28.83	1.65	46.28	5.07
	0.01	44.28	4.63	71.13	9.34
	0.001	72.3	5.36	97.12	16.56
	0.0001	106.24	10.8	108.84	2.89
	0.00001	118.64	11.64	108.4	6.58
	0.000001	101.22	26.52	121.11	11.03
	0.0000001	99.51	20.19	116.5	4.98
	0.00000001	111.26	23.8	109.78	10.85
AD-2123162.2	10	16.79	1.83	33.15	3.2
	1	18.85	3.37	36.76	2.19
	0.1	27.84	2.27	50.04	4.48
	0.01	41.34	5.9	67.11	6.33
	0.001	68.29	6.89	98.95	7.36
	0.0001	97.14	10.67	108.93	12.16
	0.00001	96.09	14.81	132.24	10.69
	0.000001	93.98	9.82	112.27	19
	0.0000001	95.78	11.92	113.34	21.24
	0.00000001	113.77	26.24	99.4	19.8
AD-2217258.1	10	17.97	2.71	34.28	2.79
	1	30.08	4.29	46.06	4.45
	0.1	31.22	3.51	58.69	5.25
	0.01	61.22	4.65	105.17	8.43
	0.001	87.15	5.85	111.06	6.69
	0.0001	94.89	6.83	113.64	13.41
	0.00001	92.09	13.73	126.66	10.96
	0.000001	89.69	4.71	113.91	13.98
	0.0000001	92.66	3.68	104.3	8.95
	0.00000001	96.54	10.99	113.69	4.03

Example 3. *In vivo* Screening in Mice

A study was performed in PXB-mice. Mice were dosed with a single injection of 5 mg/kg of AD-2217254.2, AD-2217251.2, AD-2217248.2, AD-2217250.2 , AD-2217245.2, AD-2217252.2, AD-2217253.2, AD-2217246.2, AD-2217262.2, AD-2217258.2, AD-2217255.2, AD-2217257.2, 10 mg/kg 3 times per week of AD-2123142.6, 10 mg/kg 2 times per week of AD-2123142.6, or PBS (control) by subcutaneous injection (n=4 per group). A liver sample was collected on Day 21 and analyzed for mRNA and protein levels. mRNA levels were measured by hGRB14 qPCR and protein levels were measured by LC-MS. Table 13 shows the average percent mRNA remaining on Day 21.

Table 13. Average Percent Remanining of GRB14 mRNA

Duplex	Dose	Frequency	Avg % mRNA remaining	SD
PBS	0mpk	Once	100.1	4.4
AD-2217254.2	5mpk	Once	46.5	13.8
AD-2217251.2	5mpk	Once	59.1	11.6
AD-2217248.2	5mpk	Once	68.0	29.6
AD-2217250.2	5mpk	Once	84.8	22.0
AD-2217245.2	5mpk	Once	44.9	8.3
AD-2217252.2	5mpk	Once	50.8	14.8
AD-2217253.2	5mpk	Once	86.9	26.0
AD-2217246.2	5mpk	Once	55.4	11.6
AD-2217262.2	5mpk	Once	57.8	6.8
AD-2217258.2	5mpk	Once	66.5	16.2
AD-2217255.2	5mpk	Once	72.0	19.5
AD-2217257.2	5mpk	Once	54.3	8.8
AD-2123142.6	10mpk	3x/week	39.7	2.6
AD-2123142.6	10mpk	2x/week	56.6	20.6

FIG. 1 shows the percent of GRB14 mRNA and protein remaining, respectively, relative to the PBS mean of AD-2217245 (5 mpk), AD-2217246 (5 mpk), AD-2217252 (5 mpk), AD-2217262 (5 mpk), and AD-213142 (10 mpk x3).

Example 4. *In vivo* Screening in Non-Human Primates

Duplexes AD-2217245, AD-2217246, AD-2217252, AD-2217257, and AD-2217262 with human/cynologous cross-reactivity were further investigated for their effectiveness in non-human primates. A single dose of 3 mg/kg of AD-2217245, AD-2217246, AD-2217252, AD-2217257, and AD-2217262 was subcutanesouly administered to cynologous monkeys. A single dose of 20 mg/kg of AD-2217245 was also subcutanesouly administered to cynologous monkeys. The experimental design is shown in Table 14. Sera and tissue samples were collected at Days 22 and 57.

mRNA was extracted from liver tissue by a magnetic bead-based extraction method. Taqman probe-based qPCR was used to quantify GRB14 mRNA which was normalized to the geometric mean of a housekeeping gene. Targeted quantitation of GRB14 protein in cynomolgus monkey liver was performed via liquid chromatography coupled to mass spectrometer (LC-MS). The signature peptide sequence selected for quantitation was ALDVPSDITAR (SEQ ID NO: 8855).

FIG. 2 shows the effect of administration of a single 20 mg/kg dose and 3 mg/kg dose of the selected duplexes on the level of GRB14 mRNA at Day 22 post-dose.

FIG. 3 shows the effect of administration of a single 20 mg/kg dose and 3 mg/kg dose of the selected duplexes on the level of GRB14 protein at Day 22 and Day 57 post-dose.
AD-2217245 at 3 mg/kg gave a protein knockdown of 89% at Day 22 and 80% at Day 57. AD-2217245 at 20 mg/kg gave a protein knockdown of 92% at Day 22 and Day 57.

Table 14. Experimental Design

	Dose (mg/kg)	Dose Volume (mL/kg)	Dose Concentration (mg/mL)	No. of Animals
Control	0	1	0	3
AD-2217245	20	1	20	3
AD-2217245	3	1	3	3
AD-2217246	3	1	3	3
AD-2217252	3	1	3	3
AD-2217257	3	1	3	3
AD-2217262	3	1	3	3

Example 5. *In vivo* Screening in Mouse Models for Diabetes and Obesity

Additional siRNAs were designed, synthesized, and prepared using methods known in the art and described above in Example 1. siRNAs targeting the mouse GRB14 gene (NCBI reference NM_016719.1) were also designed using custom R and Python scripts. The mouse NM_016719.1 mRNA has a length of 1978 bases. A detailed list of the additional unmodified sense and antisense strand sequences of GRB14 dsRNA agents targeting NM_016719.1 mRNA are shown in Table 15. A detailed list of the additional modified sense and antisense strand sequences of GRB14 dsRNA agents targeting NM_016719.1 mRNA are shown in Table 16.

Table 15. Unmodified Sense and Antisense Strand Sequences of GRB14 dsRNA Agents

Duplex ID	Sense Strand Sequence 5' to 3'	SEQ ID NO	Range	Antiense Strand Sequence 5' to 3'	SEQ ID NO	Range
AD-1363978	CUUUUGUACUGUCAAUGAGUA	8840	1570-1590	UACUCAUUGACAGUACAAAAGUU	8843	1568-1590
AD-1364167	UUGCAAGCUGAAGCAUUACUA	8841	1733-1753	UAGUAAUGCUUCAGCUUGCAAGG	8844	1731-1753
AD-1364168	UGCAAGCUGAAGCAUUACUGA	8842	1734-1754	UCAGUAAUGCUUCAGCUUGCAAG	8845	1732-1754

Table 16. Modified Sense and Antisense Strand Sequences of GRB14 dsRNA Agents

Duplex Name	Sense Strand Sequence 5' to 3'	SEQ ID NO	Antiense Strand Sequence 5' to 3'	SEQ ID NO	mRNA target sequence	SEQ ID NO
AD-1363978	csusuuugUfaCfUfGfucaaugaguaL96	8846	VPusAfscucAfuUfGfacagUfaCfaaaagsusu	8849	AACUUUUGUACUGUCAAUGAGUC	8852
AD-1364167	ususgcaaGfcUfGfAfagcauuacuaL96	8847	VPusAfsguaAfuGfCfuucaGfcUfugcaasgsg	8850	CCUUGCAAGCUGAAGCAUUACUG	8853
AD-1364168	usgscaagCfuGfAfAfgcauuacugaL96	8848	VPusCfsaguAfaUfGfcuucAfgCfuugcasasg	8851	CUUGCAAGCUGAAGCAUUACUGU	8854

dsRNA agents targeting mouse GRB14 were further evaluated for efficacy *in vivo* in genetically obese mice (Ob/Ob). Ob/Ob mice were administered 1 mg/kg of AD-1363978 (siRNA 1), AD-1364167 (siRNA 2), and AD-1364168 (siRNA 3) every 2 weeks for 2 months. The results, shown in FIG. 4A and FIG. 4B, demonstrated that GRB14 knockdown with these GalNac-sRNAs maintained low HbA1c in genetically obese mice.

dsRNA agents targeting mouse GRB14 were further evaluated for efficacy *in vivo* in high fat diet (HFD) treated mice. HFD mice were administered 1 mg/kg and 0.1 mg/kg of AD-1363978 (siRNA 1) and AD-1364167 (siRNA 2) every 2 weeks for 8 weeks. A Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was taken at week 8. The results, shown in FIG. 5A and FIG. 5B, demonstrated that GRB14 knockdown with these GalNac-sRNAs improved HOMA-IR in HFD mice. In FIG. 5A, *=p<0.05 and **=p<0.01.

dsRNA agents targeting mouse GRB14 were further evaluated for efficacy *in vivo* in diet induced obese (DIO) mice. DIO mice were administered 10 mg/kg of AD-1363978 (siRNA 1) and AD-1364167 (siRNA 2) every 2 weeks for 8 weeks. Lean mice were used as a control. Glucose tolerance and insulin tolerance tests were run at week 8 and week 9, respectively, with glucose and insulin administered in proportion to body weight. The final body weight of the mice was taken at week 11. The results, shown in FIG. 6A, FIG. 6B, and FIG. 6C, demonstrated that knockdown of GRB14 with these GalNac-sRNAs improved glycemia and insulin sensitivity without weight gain.

GRB14 SEQUENCES

SEQ ID NO: 1
>NM_004490.3 Homo sapiens growth factor receptor bound protein 14 (GRB14), transcript variant 1, mRNA

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SEQ ID NO: 3
>NM_001303422.2 Homo sapiens growth factor receptor bound protein 14 (GRB14), transcript variant 2, mRNA
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SEQ ID NO: 5
>NM_016719.1 Mus musculus growth factor receptor bound protein 14 (Grb14), mRNA
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SEQ ID NO: 6
>Reverse Complement of SEQ ID NO: 5
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CAGTTTGGCTAAACAGCCATCCTAGCACAGTAATGCTTCAGCTTGCAAGGAAGGACCCCCCTGTTGAGCTGGTAGAA
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SEQ ID NO: 7
>NM_031623.1 Rattus norvegicus growth factor receptor bound protein 14
(Grb14), mRNA
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SEQ ID NO: 8
>Reverse Complement of SEQ ID NO: 7
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AAGCGAAGAAAGGCTGGGGTCCAGC

SEQ ID NO: 9
>XM_015110244.2 PREDICTED: Macaca mulatta growth factor receptor bound protein 14 (GRB14), transcript variant X1, mRNA
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GGGACTGTCATGGCGGCCCAGCAACAGCTTAGGTGATCTCAGATGGCAGAGCAGGAAGAATGCAAGGGTATGAGGGT
CAGGGCTGCGCAGACCCCTGTCCCGCCTGCGGTCCTCCCGGCAAGCCCAGGGGGAGAGCCCGCTCTGCTGGGTCTCC
GCCTCCAGCGGCGCCGGGCCGCCCAGACCCTGGGCTCAGTCTTGCGCCCCGGTGCCCACCTGGGGAGGCGGCGGTCC
CGGCCTCGCGTCCCGGATCGGACGGCGCGGGAGCGATGCCAGCGGCCCCGAGCGCCCCGGGCCACGCGCGGGGCCGG
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SEQ ID NO: 10
>Reverse Complement of SEQ ID NO: 9
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SEQ ID NO: 11
>XM_028830779.1 PREDICTED: Macaca mulatta growth factor receptor bound
protein 14 (GRB14), transcript variant X2, mRNA
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CCTTAGAAAAAAATTGA

SEQ ID NO: 12
>Reverse Complement of SEQ ID NO: 11
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SEQ ID NO: 13
>XM_015110245.2 PREDICTED: Macaca mulatta growth factor receptor bound protein 14 (GRB14), transcript variant X3, mRNA

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GCATGAGTTTGAGTGCAAGAAGAGTCACTCTGCCTGCAATAACGCCAATAATTCTACAGAAAAGGGTGATTAAAGTG
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SEQ ID NO: 14
>Reverse Complement of SEQ ID NO: 13
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SEQ ID NO: 15
>XM_008258679.2 PREDICTED: Oryctolagus cuniculus growth factor receptor bound protein 14 (GRB14), transcript variant X1, mRNA

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SEQ ID NO: 16
>Reverse Complement of SEQ ID NO: 15
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SEQ ID NO: 17
>XM_017342897.1 PREDICTED: Oryctolagus cuniculus growth factor receptor bound protein 14 (GRB14), transcript variant X2, mRNA

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SEQ ID NO: 18
>Reverse Complement of SEQ ID NO: 17

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SEQ ID NO: 19
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SEQ ID NO: 20
>Reverse Complement of SEQ ID NO: 19
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We claim:

1. A double stranded ribonucleic acid (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell, wherein said dsRNA agent comprises a sense strand and an antisense strand forming a double stranded region, wherein said antisense strand comprises a region of complementarity to an mRNA encoding GRB14 which comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from any one of the antisense sequences listed in any one of Tables 2-7 or 15-16.

2. The dsRNA agent of claim 1, wherein said dsRNA agent comprises at least one modified nucleotide.

3. The dsRNA agent of claim 1 or 2, wherein substantially all of the nucleotides of the sense strand comprise a modification.

4. The dsRNA agent of claim 1 or 2, wherein substantially all of the nucleotides of the antisense strand comprise a modification.

5. The dsRNA agent of claim 1 or 2, wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand comprise a modification.

6. A double stranded RNA (dsRNA) agent for inhibiting expression of growth factor receptor bound protein 14 (GRB14) in a cell, wherein the double stranded RNA agent comprises a sense strand and an antisense strand forming a double stranded region,

wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16,

wherein substantially all of the nucleotides of the sense strand and substantially all of the nucleotides of the antisense strand are modified nucleotides, and

wherein the sense strand is conjugated to a ligand attached at the 3'-terminus.

7. The dsRNA agent of claim 6, wherein all of the nucleotides of the sense strand comprise a modification.

8. The dsRNA agent of claim 6, wherein all of the nucleotides of the antisense strand comprise a modification.

9. The dsRNA agent of claim 6, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand comprise a modification.

10. The dsRNA agent of any one of claims 2-9, wherein the at least one modified nucleotide is selected from the group consisting of a deoxy-nucleotide, a 3'-terminal deoxy-thymine (dT) nucleotide, a 2'-O-methyl modified nucleotide, a 2'-fluoro modified nucleotide, a 2'-deoxy-modified nucleotide, a locked nucleotide, an unlocked nucleotide, a conformationally restricted nucleotide, a constrained ethyl nucleotide, an abasic nucleotide, a 2'-amino-modified nucleotide, a 2'-O-allyl-modified nucleotide, 2'-C-alkyl-modified nucleotide, a 2'-methoxyethyl modified nucleotide, a 2'-O-alkyl-modified nucleotide, a morpholino nucleotide, a phosphoramidate, a non-natural base comprising nucleotide, a tetrahydropyran modified nucleotide, a 1,5-anhydrohexitol modified nucleotide, a cyclohexenyl modified nucleotide, a nucleotide comprising a phosphorothioate group, a nucleotide comprising a methylphosphonate group, a nucleotide comprising a 5'-phosphate, a nucleotide comprising a 5'-phosphate mimic, a glycol modified nucleotide, and a 2-O-(N-methylacetamide) modified nucleotide, and combinations thereof.

11. The dsRNA agent of claim 10, wherein the at least one modified nucleotide is a 2'-O-methyl and/or a 2'-fluoro modification.

12. The dsRNA agent of any one of claims 1-11, wherein the region of complementarity is at least 17 nucleotides in length.

13. The dsRNA agent of any one of claims 1-12, wherein the region of complementarity is 19 to 30 nucleotides in length.

14. The dsRNA agent of claim 13, wherein the region of complementarity is 19-25 nucleotides in length.

15. The dsRNA agent of claim 14, wherein the region of complementarity is 21 to 23 nucleotides in length.

16. The dsRNA agent of any one of claims 1-15, wherein each strand is no more than 30 nucleotides in length.

17. The dsRNA agent of any one of claims 1-16, wherein each strand is independently 19-30 nucleotides in length.

18. The dsRNA agent of claim 17, wherein each strand is independently 19-25 nucleotides in length.

19. The dsRNA agent of claim 17, wherein each strand is independently 21-23 nucleotides in length.

20. The dsRNA agent of any one of claims 1-19, wherein at least one strand comprises a 3' overhang of at least 1 nucleotide.

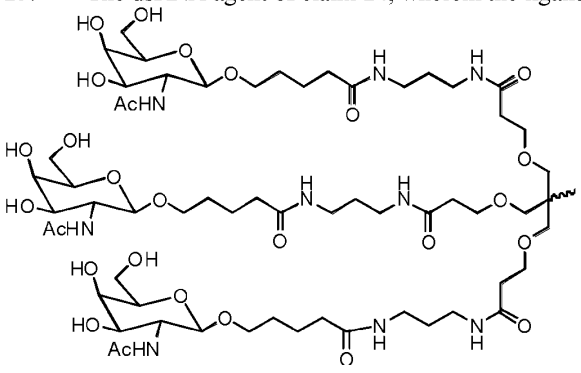
21. The dsRNA agent of any one of claim 20, wherein at least one strand comprises a 3' overhang of at least 2 nucleotides.

22. The dsRNA agent of any one of claims 1-5 and 10-21, further comprising a ligand.

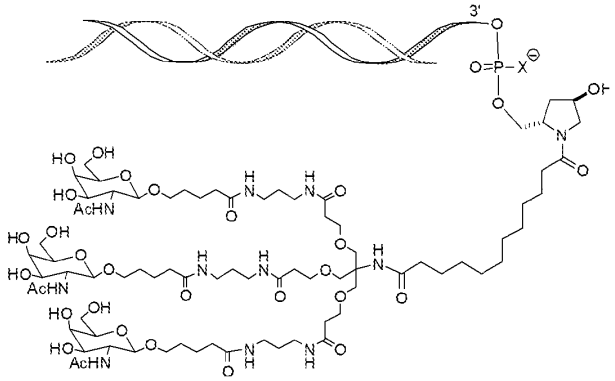
23. The dsRNA agent of claim 22, wherein the ligand is conjugated to the 3' end of the sense strand of the dsRNA agent.

24. The dsRNA agent of claim 6, 22, or 23, wherein the ligand is an N-acetylgalactosamine (GalNAc) derivative.

25. The dsRNA agent of claim 24, wherein the ligand is



26. The dsRNA agent of claim 25, wherein the dsRNA agent is conjugated to the ligand as shown in the following schematic



and, wherein X is O or S.

27. The dsRNA agent of claim 26, wherein the X is O.

28. The dsRNA agent of any one of claims 1-27, wherein

(a) the sense strand comprises the nucleotide sequence CAAAACUUUCGUACUGUCAAA (SEQ ID NO: 8770) and the antisense strand comprises the nucleotide sequence UUUGACAGUACGAAAGUUUUGGG (SEQ ID NO: 8784);

(b) the sense strand comprises the nucleotide sequence AAGACUUGGAUUGACUUUACA (SEQ ID NO: 8771) and the antisense strand comprises the nucleotide sequence UGUAAAGUCAAUCCAAGUCUUUG (SEQ ID NO: 8785);

(c) the sense strand comprises the nucleotide sequence UUGACUUUACAUUCAUCAUUA (SEQ ID NO: 8777) and the antisense strand comprises the nucleotide sequence UAAUGATGAAUGUAAAGUCAAUC (SEQ ID NO: 8791);

(d) the sense strand comprises the nucleotide sequence UUAUGCCAAAUAUGAGUUCUA (SEQ ID NO: 8781) and the antisense strand comprises the nucleotide sequence UAGAACTCAUATUUGGCAUAAUU (SEQ ID NO: 8795);

(e) the sense strand comprises the nucleotide sequence UGCAAGUUGAAACAUUAUUGA (SEQ ID NO: 8783) and the antisense strand comprises the nucleotide sequence UCAATAAUGUUTCAACUUGCAAG (SEQ ID NO: 8797); or

(f) the sense strand comprises the nucleotide sequence UAUCCUGAAAUUCAUGGUUUA (SEQ ID NO: 7595) and the antisense strand comprises the nucleotide sequence UAAACCAUGAATUUCAGGAUAUG (SEQ ID NO: 7863).

29. The dsRNA agent of any one of claims 1-28, wherein

(a) the sense strand consists of the nucleotide sequence CAAAACUUUCGUACUGUCAAA (SEQ ID NO: 8770) and the antisense strand consists of the nucleotide sequence UUUGACAGUACGAAAGUUUUGGG (SEQ ID NO: 8784);

(b) the sense strand consists of the nucleotide sequence AAGACUUGGAUUGACUUUACA (SEQ ID NO: 8771) and the antisense strand consists of the nucleotide sequence UGUAAAGUCAAUCCAAGUCUUUG (SEQ ID NO: 8785);

(c) the sense strand consists of the nucleotide sequence UUGACUUUACAUUCAUCAUUA (SEQ ID NO: 8777) and the antisense strand consists of the nucleotide sequence UAAUGATGAAUGUAAAGUCAAUC (SEQ ID NO: 8791);

(d) the sense strand consists of the nucleotide sequence UUAUGCCAAAUAUGAGUUCUA (SEQ ID NO: 8781) and the antisense strand consists of the nucleotide sequence UAGAACTCAUATUUGGCAUAAUU (SEQ ID NO: 8795);

(e) the sense strand consists of the nucleotide sequence UGCAAGUUGAAACAUUAUUGA (SEQ ID NO: 8783) and the antisense strand consists of the nucleotide sequence UCAATAAUGUUTCAACUUGCAAG (SEQ ID NO: 8797); or

(f) the sense strand consists of the nucleotide sequence UAUCCUGAAAUUCAUGGUUUA (SEQ ID NO: 7595) and the antisense strand consists of the nucleotide sequence UAAACCAUGAATUUCAGGAUAUG (SEQ ID NO: 7863).

30. The dsRNA agent of any one of claims 1-28, wherein

(a) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8798 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8812;

(b) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8799 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8813;

(c) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8805 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8819;

(d) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8809 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8823;

(e) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8811 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8825; or

(f) the sense strand comprises the sequence and all the modifications of SEQ ID NO: 8131 and the antisense strand comprises the sequence and all the modifications of SEQ ID NO: 8399.

31. The dsRNA agent of claim 1, wherein the region of complementarity comprises any one of the antisense sequences in Tables 2-7 or 15-16.

32. The dsRNA agent of claim 31, wherein the dsRNA agent is selected from the group consisting of AD-2217254, AD-2217251, AD-2217248, AD-2217250, AD-2217245, AD-2217252, AD-2217253, AD-2217246, AD-2217262, AD-2217258, AD-2217255, AD-2217257, or AD-2123142.

33. The dsRNA agent of any one of claims 2-29, wherein the at least one modified nucleotide is selected from the group consisting of LNA, HNA, CeNA, 2′-methoxyethyl, 2′-O-alkyl, 2′-O-allyl, 2′-C- allyl, 2′-fluoro, 2'-O-methyl, 2′-deoxy, and combinations thereof.

34. The dsRNA agent of claim 33, wherein the at least one modified nucleotide is a 2′-O-methyl and/or a 2′-fluoro modification.

35. The dsRNA agent of any one of claims 1-33, wherein the dsRNA agent further comprises at least one phosphorothioate or methylphosphonate internucleotide linkage.

36. The dsRNA agent of claim 35, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 3'-terminus of one strand.

37. The dsRNA agent of claim 36, wherein said strand is the antisense strand.

38. The dsRNA agent of claim 36, wherein said strand is the sense strand.

39. The dsRNA agent of claim 35, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at the 5'-terminus of one strand.

40. The dsRNA agent of claim 39, wherein said strand is the antisense strand.

41. The dsRNA agent of claim 39, wherein said strand is the sense strand.

42. The dsRNA agent of claim 35, wherein the phosphorothioate or methylphosphonate internucleotide linkage is at both the 5'- and 3'-terminus of one strand.

43. The dsRNA agent of any one of claims 1-42, wherein the base pair at the 1 position of the 5′-end of the antisense strand of the duplex is an AU base pair.

44. The dsRNA agent of any one of claims 1-43, wherein the sense strand has a total of 21 nucleotides and the antisense strand has a total of 23 nucleotides.

45. A double stranded ribonucleic acid (dsRNA) agent for inhibiting the expression of growth factor receptor bound protein 14 (GRB14) in a cell, wherein the dsRNA agent comprises a sense strand and an antisense strand forming a double stranded region,

wherein the sense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of any one of the sense sequences listed in any one of Tables 2-7 or 15-16 and the antisense strand comprises at least 15 contiguous nucleotides differing by no more than 3 nucleotides from the nucleotide sequence of any one of the antisense sequences listed in any one of Tables 2-7 or 15-16,

wherein substantially all of the nucleotides of the sense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification and a 2'-fluoro modification,

wherein the sense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus,

wherein substantially all of the nucleotides of the antisense strand comprise a modification selected from the group consisting of a 2'-O-methyl modification, a 2'-fluoro modification, and a deoxy-nucleotide,

wherein the antisense strand comprises two phosphorothioate internucleotide linkages at the 5'-terminus and two phosphorothioate internucleotide linkages at the 3'-terminus, and

wherein the sense strand is conjugated to one or more GalNAc derivatives attached through a monovalent, bivalent or trivalent branched linker at the 3'-terminus.

46. The dsRNA agent of claim 45, wherein all of the nucleotides of the sense strand and all of the nucleotides of the antisense strand are modified nucleotides.

47. The dsRNA agent of any one of claims 1, 45, or 46, wherein the region of complementarity comprises any one of the antisense sequences listed in Tables 2-7 or 15-16.

48. The dsRNA agent of any one of claims 1-47, wherein the sense strand and the antisense strand comprise nucleotide sequences selected from the group consisting of the nucleotide sequences of any one of the agents listed in Tables 2-7 or 15-16.

49. The dsRNA agent of any one of claims 1-48, wherein the dsRNA agent targets a hotspot region of an mRNA encoding GRB14.

50. A dsRNA agent that targets a hotspot region of a growth factor receptor protein 14 (GRB14) mRNA.

51. A cell containing the dsRNA agent of any one of claims 1-50.

52. A vector encoding at least one strand of the dsRNA agent of any one of claims 1-50.

53. A pharmaceutical composition for inhibiting expression of the growth factor receptor protein 14 (GRB14) gene comprising the dsRNA agent of any one of claims 1-50.

54. The pharmaceutical composition of claim 53, wherein the dsRNA agent is formulated in an unbuffered solution.

55. The pharmaceutical composition of claim 54, wherein the unbuffered solution is saline or water.

56. The pharmaceutical composition of claim 53, wherein the agent is formulated with a buffered solution.

57. The pharmaceutical composition of claim 56, wherein said buffered solution comprises acetate, citrate, prolamine, carbonate, or phosphate or any combination thereof.

58. The pharmaceutical composition of claim 56, wherein the buffered solution is phosphate buffered saline (PBS).

59. A method of inhibiting growth factor receptor bound protein 14 (GRB14) expression in a cell, the method comprising introducing into the cell the dsRNA agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby inhibiting expression of GRB14 in the cell.

60. The method of claim 59, wherein said cell is within a subject.

61. The method of claim 60, wherein the subject is a human.

62. The method of any one of claims 59-61, wherein the GRB14 expression is inhibited by at least 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or to below the level of detection of GRB14 expression.

63. The method of claim 61, wherein the human subject has a GRB14-associated disease, disorder, or condition.

64. The method of claim 63, wherein the GRB14-associated disease, disorder, or condition is diabetes.

65. The method of claim 64, wherein the diabetes is type 2 diabetes.

66. The method of claim 64, wherein the diabetes is type 1 diabetes.

67. The method of claim 63, wherein the GRB14-associated disease, disorder, or condition is prediabetes.

68. The method of claim 63, wherein the GRB14-associated disease, disorder, or condition is insulin resistance.

69. The method of claim 63, wherein the GRB14-associated disease, disorder, or condition is selected from the group consisting of obesity, diabetic neuropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

70. A method of inhibiting the expression of GRB14 in a subject, the method comprising administering to the subject a therapeutically effective amount of the dsRNA agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby inhibiting the expression of GRB14 in said subject.

71. A method of treating a subject having a GRB14-associated disease, disorder, or condition, comprising administering to the subject a therapeutically effective amount of the agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby treating the subject having the GRB14-associated disease, disorder, or condition.

72. A method of preventing at least one symptom in a subject having a GRB14-associated disease, disorder, or condition comprising administering to the subject a prophylactically effective amount of the agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby preventing at least one symptom in the subject having the GRB14-associated disease, disorder, or condition.

73. The method of claim 71 or 72, wherein the GRB14-associated disease, disorder, or condition is diabetes.

74. The method of claim 73, wherein the diabetes is type 2 diabetes.

75. The method of claim 74, wherein the diabetes is type 1 diabetes.

76. The method of claim 71 or 72, wherein the GRB14-associated disease, disorder, or condition is prediabetes.

77. The method of claim 71 or 72, wherein the GRB14-associated disease, disorder, or condition is insulin resistance.

78. The method of claim 71 or 72, wherein the GRB14-associated disease, disorder, or condition is selected from the group consisting of obesity, diabetic neuropathy, diabetic nephropathy, diabetic vasculopathy, diabetic retinopathy, hypertension, dyslipidemia, atherosclerosis, coronary heart disease, and stroke.

79. A method of reducing risk of a subject developing type 2 diabetes, the method comprising administering to the subject a prophylactically effective amount of the dsRNA agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby reducing the risk of the subject developing type 2 diabetes.

80. A method of increasing insulin sensitivity in a subject, the method comprising administering to the subject a therapeutically effective amount of the dsRNA agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby increasing insulin sensitivity in the subject.

81. A method of reversing type 2 diabetes in a subject, the method comprising administering to the subject a therapeutically effective amount of the dsRNA agent of any one of claims 1-50, or a pharmaceutical composition of any one of claims 53-58, thereby reversing type 2 diabetes in the subject.

82. The method of any one of claims 60-81, wherein the subject is obese.

83. The method of any one of claims 60-82, further comprising administering an additional therapeutic to the subject.

84. The method of any one of claims 60-83, wherein the dsRNA agent is administered to the subject at a dose of about 0.01 mg/kg to about 10 mg/kg or about 0.5 mg/kg to about 50 mg/kg.

85. The method of any one of claims 60-84, wherein the agent is administered to the subject intravenously, intramuscularly, or subcutaneously.

86. The method of any one of claims 60-85, further comprising determining a level of GRB14 mRNA or protein in the subject.